

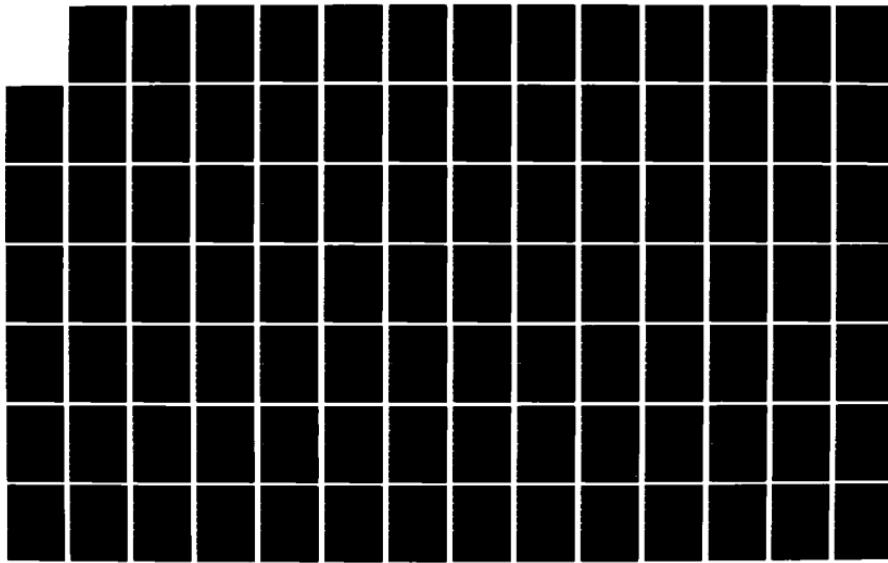
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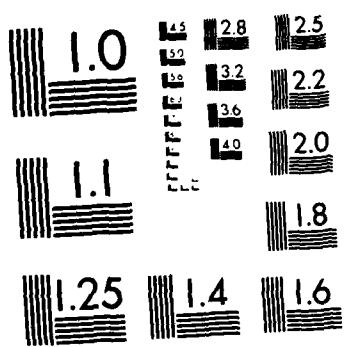
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Biological Effects
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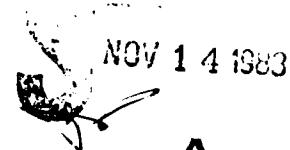
Volume VII, Number 2-4
(July Thru December 1982)

July 1983

A Digest of Current Literature

A Quarterly Publication Produced for
Office of Naval Research

INFORMATION VENTURES, INC.



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**Biological Effects
of Nonionizing Electromagnetic Radiation**

A Digest of Current Literature

**A Quarterly Publication Produced for
Office of Naval Research**

Literature Selected and Abstracted

by

*Information Ventures, Inc.
1500 Locust Street
Philadelphia, Pa 19102*

Bruce H. Kleinstein, Ph.D., J.D., Project Manager

The views and conclusions contained in this documentation are those of the author and should not be interpreted as necessarily representing the official policies, either expressed or implied, of the Office of Naval Research.

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density, specific absorption rate, drugs or other stimuli, exposure duration and regime, and end point are included in each abstract.

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Biological Effects of Nonionizing Electromagnetic Radiation

July, 1983 Volume VII, Number 2-4

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Preface

Biological Effects of Nonionizing Electromagnetic Radiation is a publication researched and prepared by Information Ventures, Inc. under contract to the Office of Naval Research.

This digest serves as a vehicle through which current documentation of research highlights on the biological effects and health implications of nonionizing electromagnetic radiation (microwave and other radio frequency radiation) is compiled, condensed, and disseminated on a regular basis. The effects of electric and magnetic fields (static and alternating) and research on medical applications of these nonionizing electromagnetic radiations are also included.

Biological Effects of Nonionizing Electromagnetic Radiation is intended to be a highly useful current awareness tool for scientists engaged in research or related activities. The great number and diversity of relevant publications make imperative the availability of the service to persons whose work requires that they keep abreast of current developments in the field.

Biological Effects of Nonionizing Electromagnetic Radiation is published quarterly. The issues of Volume VII and future volumes will include materials received during the preceding three months. Each issue contains abstracts of current English and foreign-language research literature, current research summaries, news items and announcements, and information on relevant meetings and conferences. Subject and author indices are provided for all literature abstracts to facilitate specific search and reference use. Journals, books and conference proceedings are used as sources for this publication. Materials for which full text is not available will be included as summary abstracts. Announcements and other materials submitted for publication should be addressed to: Dr. Bruce H. Kleinstein, Information Ventures, Inc., 1500 Locust Street, Philadelphia, PA 19102.

The digest was first published in 1974 under the title "Biological Effects of Electromagnetic Radiation." Since 1976 it has been published under the present title. Previous issues can be obtained from the National Technical Information Service.

Abbreviations and Acronyms

| | |
|--|---------------------------------------|
| A - amp, ampere | m - milli- |
| ANSI - American National Standards Institute | M - mega- |
| C - centigrade | u - micro- |
| cm - centimeter(s) | min - minute(s) |
| cps - cycles per second | mo - month(s) |
| dB - decibel(s) | n - nano- |
| EPA - Environmental Protection Agency | NIH - National Institutes of Health |
| eV - electron volt | NIOSH - National Institute for Occu- |
| F - fahrenheit | pational Safety and Health |
| FAA - Federal Aviation Administration | NTIS - National Technical Information |
| FDA - Food and Drug Administration | Service |
| g - gram(s) | Oe - oersted(s) |
| G - gauss | OSHA - Occupational Safety and Health |
| GHz - gigahertz | Administration |
| HHS - Department of Health and Human Services | rad - radiation absorbed dose(s) |
| hr - hour(s) | R - roentgen(s) |
| Hz - hertz | rpm - revolutions per minute |
| ip - intraperitoneal | sec - second(s) |
| ISM - industrial, scientific, medical | sc - subcutaneous |
| IU - international unit(s) | V - volts |
| iv - intravenous | VA - Veterans Adminstration |
| J - joule(s) | W - watt(s) |
| k - kilo- | WHO - World Health Organization |
| l - liter(s) | wk - week(s) |
| m - meter(s) | wt - weight |
| | x - times |
| | yr - year(s) |

NEWS ITEMS

TERMINAL Tedium: CERTAIN CLERKS ARE DENOUNCING THEIR COMPUTERS

(J. Andrew, *The Wall Street Journal*, May 6, 1983) Workers in automated offices are frequently bothered by backaches and headaches from sitting in front of a terminal for long hours. Such physical complaints seem to be caused by a combination of improper lighting, uncomfortable seating arrangements and insufficient rest periods. Also at issue is whether microwave radiation emitted by the cathode-ray tubes inside terminals might cause illnesses - cancer and cataracts in particular. The tubes generally emit less radiation than television sets, but one sits closer to them. Studies so far have failed to establish any health hazard, although VDTs haven't been in general use long enough for health issues to be resolved conclusively. At least two states, Maine and Massachusetts, are considering legislation addressing some of the health concerns about video display terminals. The proposals would require, among other things, regular inspection of terminals, free eye examinations for frequent users and certain rest breaks during the working day. Rep. Edith Bouillier, the sponsor of the Maine legislation, predicts further controversy over the health effects of video display terminal usage. She believes that in four or five years it will become a workers' compensation issue.

BOOK REVIEW: Environmental Health Criteria 16: Radio-frequency and Microwaves. World Health Organization, Geneva, 1981.

A critical review of this document (see abstract 0066 of BENER Digest vol 6, number 1) is presented. The reviewer comments that the publication is rather unbalanced and does not come up to the high scientific caliber and accuracy of the usual WHO publications.

S. M. Michaelson, *Radiat Res*, 92:217-219, 1982

TWO SICKLE-CELL RESEARCHERS STUDY ELECTRICAL TECHNIQUE

(L. Herskowitz, *Philadelphia Inquirer*, May 3, 1983) Researchers at Children's Hospital of Philadelphia and the University of Pennsylvania have developed the first nonchemical approach to treating sickle-cell anemia. The technique uses very short, pulsing electrical charges to alter the shape and consistency of sickle-shaped red blood cells. The technique was reported in the April 22 issue of *Science* magazine by Dr. Toshio Asakura, a member of the Children's Hospital department of pediatrics and of Penn's departments of biochemistry and biophysics and by Dr. Shiro Takashima, a member of Penn's department of bioengineering and its school of engineering and applied science. To apply electricity to the cells, the re-

searchers attached small electrodes to each side of a microscope slide that held blood taken from people with sickle-cell disease. Once a second, a small generator delivered a 200-volt electrical pulse lasting one-thousandth of a second. After three or four minutes, the sickle-cell's shape changes to a normal round shape. The researchers believe that the electrical field punches holes in the red blood cells' membranes allowing water molecules to seep into the cells and puff them up. They also say there is preliminary evidence that the treatment partially reverses the aggregation of the hemoglobin inside the cell. The researchers say it is not clear whether the technique will work on humans. The body may not be able to withstand the very large voltage required to treat large amounts of blood. Further, the electrical field may cause irreversible swelling or eventually lead to hemolysis.

CATTLE SEEM UNAFFECTED BY HIGH-VOLTAGE POWER LINE

(K.M. Reese, C&EN News, January 3, 1983) A study of dairy cattle living near a high-voltage power line in Minnesota showed no significant effects on milk production and reproduction. The 400,000-volt line cuts across 180 miles of farmland, from Delano to the North Dakota border. The Minnesota Environmental Quality Board authorized the \$89,000 study to see if ions and electric fields generated by the line might harm the health of humans and animals. The power line is owned by the Cooperative Power Association and the United Power Association. Chief investigator on the project was statistician Frank Martin of the University of Minnesota. Martin and his colleagues studied the records of the Dairy Herd Improvement Association. The data covered 500 herds within 10 miles to either side of the power line and extended from October 1976, two years before the line went into operation, to September 1982. Dairy farms within 10 miles of the line were divided into six zones. Zone 1 included farms within a quarter mile of the line; zone 6 included those six to ten miles from it. The outer zones, especially zone 6, were considered control areas, unexposed to the influence of the power line. Over the period of the study, herds within a quarter mile of the line showed "an acceptable 8% increase in milk production." Times between births of calves, rates of removal of cows from herds because of reproductive problems, and the incidence of recorded abortions "were no higher near the power line than at six to 10 miles away." The study assumed that any harmful effects of the power line would exist throughout the zone closest to it. If the power line affected only a very few of the farms within a quarter mile of the line, this study would not have caught it. Farms having serious problems were found both close to and far from the power line. Farms showing excellent increases in production also were found in both areas.

News Items

Biological Effects of Nonionizing Electromagnetic Radiation VII(2-4), July 1983

HEALTH HAZARDS AND PSYCHOPHYSIOLOGICAL EFFECTS FROM LOW-LEVEL ELECTROMAGNETIC RADIATION SYSTEMS (such as: Video Display Terminals (VDTs/VDUs), Computer programs, Advanced Aeronautics, ELF Transmitters, High-Voltage Transmission Systems). A Transcript of an International Forum. \$45.00 (post-paid). Planetary Association for Clean Energy, Inc., 100 Bronson/1001, Ottawa K1R 6G8, Canada: 613/236-6265.

The 1982 Learned Societies Conference in Ottawa presented a discussion by distinguished researchers on the state of advanced knowledge in low-level EM radiation effects on living organisms. Emphasis was on VDTs but their remarks covered research into other similar human/technological interfaces. The subjects discussed included stress symptoms, biologically significant frequency-intensity "windows", pulsed electrostatic fields, magnetic ELF fields, comparative scientific methodology between East European and Western Laboratories, and malignant pregnancy clusters among female VDT operators. Participating in the transcript were: James Beal/Martin Marietta Aerospace; Dr Robert Beck/Alpha Metrics, Inc.; Dr. Robert Becker/SUNY-Syracuse; William Bise/Pacific Northwest Center for the Study of Non-ionizing Radiation; Dr. Eldon Byrd/U.S. Naval Surface Weapons Center; David Eisen/American Newspaper Guild; Claire-Marie Fortin/Canadian Labour Congress; Dr. E. Stanton Maxey/American Board of Surgery; Dr. Russel Jaffe/senior health consultant; Robert DeMatteo/Ontario Public Service Employees Union; Dr. Glen Rein/St. Bartholomew's Hospital-London; Louis Slesin/Microwave News; Professor William Kuhns (moderator) / Communications-University of Ottawa.

CENTER RESPONDS TO INQUIRIES ON EFFECTS OF VDT'S ON PREGNANCY OUTCOMES

The National Center for Devices and Radiological Health (NCDRH) recently has been receiving inquiries as to whether "clusters" of adverse pregnancy outcomes among women who work at video display terminals (VDT's) could be caused by radiation from VDT's. The inquiries have been prompted by news media accounts such as one from Canada which reported that since VDT's were installed in the offices of a Vancouver hospital in 1978, only one of six pregnancies among women working at the machines resulted in a normal full-term birth. Over the past several years, NCDRH has tested more than 100 VDT's for radiation leakage. Results of NCDRH's current testing support the conclusion that VDT's should not pose a radiation risk to those who operate them; no evidence has been found that the levels of radiation from VDT's are responsible for adverse pregnancy outcomes. The National Research Council of the National Academy of Sciences and the National Institute for Occupational Safety and health have reached similar conclusions. Epidemiologists and statisticians at the NCDRH and at the U.S. Centers for Disease Control have noted that some "clusters" of adverse pregnancy outcomes would normally be expected on the basis of chance alone. In fact, evaluation of some of the reported "clusters" indicated that they did not establish a general pattern associating the use of VDT's with problem pregnancies. Therefore it has been concluded that the reported "clusters" of problem pregnancies among VDT users would be expected from chance alone, and it is highly unlikely that they have been caused by the low radiation emissionn levels from the machines.

Radiological Health Bulletin, 17(2):3-4, 1983

VDTs -- A NEW SOCIAL DISEASE

Health problems that have so far been associated with VDTs fall into four broad categories: alleged radiation hazard, visual disturbances, musculoskeletal difficulties, and job stress. A brief essay is presented on the above based on information supplied by Dr. Michael J. Smith of the National Institute of Occupational Safety and Health. In summary, there appears to be no radiation hazard from VDTs. Visual difficulties include irritation, fatigue, or difficulty with focus or accommodation. Minimal criteria for the visual display are: the image should not flicker; the entire display should be in sharp focus; the contrast between light and dark areas should be at least 8 to 1; the characters should be formed in a 5x7 matrix of dots at the very least; all VDTs should have brightness and contrast controls that the operator can find and adjust. Most potential health problems caused by VDTs can probably be averted by planning that takes account of the operators' needs.

The Harvard Medical School Health Letter, April 1983

FDA COMPLETES SEIZURE OF "POCKETDOC" RF SIGNAL GENERATORS

The Food and Drug Administration has seized a number of medical devices called "Pocketdoc," manufactured and distributed by Igon Corporation of Minden, Nevada. The Agency requested the seizure because the devise was found to be misbranded under the provisions of the Federal Food, Drug, and Cosmetic Act. FDA officials determined that the device was being promoted for treatment of such diverse ailments as asthma, hemorrhoids, chronic headache, chest pain, arthritis, insomnia, and whiplash. Analysis of the device showed it to be a very low power ELF (extremely low frequency) generator. A search of the scientific literature by the National Center for Devices and Radiological Health's Division of Risk Assessment revealed no published data to substantiate the labeled claims for the frequencies and power levels at which the device operates.

Radiological Health Bulletin, 17(2):4-5, 1983

**DEVELOP EDUCATIONAL GUIDELINES AND
RECOMMENDATIONS FOR HYPERTERMIA OPERATORS**

The Food and Drug Administration is seeking a contractor to interview hyperthermia equipment operators, develop methodology, analyze information and develop recommendations and guidelines for the hyperthermia equipment operators. RFP 223-83-6032 is expected to be available o/a June 20, 1983.

Commerce Business Daily, June 20, 1983

**SURVEYS OF RADIOFREQUENCY SEALER
EQUIPMENT AND OPERATOR EXPOSURE**

Sol 223-83-4260. Response date 7/28/83. Radiofrequency (RF) sealers and heaters have been used for more than 30 years, but there are no reliable, documented estimates of the number of units in present use or of the number of workers operating RF sealers. FDA and other government agencies are concerned about the potential health hazards to workers exposed to radiofrequency energy emitted from RF dielectric heaters (more widely known as RF sealers and heaters). FDA is seeking additional information about the use and means to locate this equipment at the state level, and assess the need at each site for effective control technology. The agency is also seeking the identification of suitable populations of exposed persons and is interested in feasibility studies to assess practicable epidemiologic studies. Competition will be limited to state government agencies having the regulatory authority to accomplish the project. The project includes visits to user facilities to conduct measurements of electromagnetic radiation from RF sealers where access to the premises can only be obtained by a duly authorized governmental representative.

Commerce Business Daily, May 19, 1983

**SURVEY AND TECHNICAL EVALUATION OF
HIGH POWER MICROWAVE SOURCE DEVELOPMENT**

The Office of Naval Research is conducting negotiations with Jaycor, 205 South Whiting St., Alexandria, VA 22304 for the above study.

Commerce Business Daily, May 19, 1983

**EFFECTS OF LOCAL MICROWAVE
EXPOSURE ON LOCAL TISSUE BLOOD FLOW**

Contract 68-02-3782. The EPA has contracted with the Univ. of Illinois, 809 South Wright Street, Champaign, IL 61820 for the above study.

Commerce Business Daily, May 18, 1983

AUDITORY MAGNETIC EVOKED FIELDS

Contract N00014-79-C-0383. The Office of Naval Research has contracted with the University of Colorado Medical Center, Denver, CO 80220 for the above study. Commerce Business Daily, May 10, 1983

**CONTINUATION OF RESEARCH ENTITLED "MICROWAVES,
ELECTROMAGNETIC THEORY & INFORMATION PROCESSES (JSEP)**

Contract F49620-82-C-0084-P00003. The Air Force Office of Scientific Research has contracted with Polytechnic Institute of New York, 333 Jay St., Brooklyn, NY 11201 for the above study.

Commerce Business Daily, April 18, 1983

ULTRA LOW FREQUENCY FIELDS IN NONHOMOGENEOUS MEDIA

The Office of Naval Research is conducting negotiations with Pacific Sierra Research Corp., 12340 Santa Monica Blvd., Los Angeles, CA 90025 for the above study.

Commerce Business Daily, April 6, 1983

**EXAMINE THE EFFECT OF RADIO ENERGY
ON THE OXIDATION OF ORGANIC SUBSTANCES**

The office of Naval Research is conducting negotiations with SRI International, 333 Ravenswood Ave., Menlo Park, CA 94025 for the above study.

Commerce Business Daily, April 6, 1983

MEETINGS AND CONFERENCES

SHORT COURSE HYPERTHERMIA FOR CANCER TREATMENT

Date: August 8-10, 1983

Place: Tropicana Hotel, Atlantic City

Fee: \$500 (includes lecture notes, instructional materials, refreshment breaks, and completion certificate; hotel accommodations not included)

Requests for Information: Dana Carpenter, Course Coordinator, Cheung Associates, Inc., 5026 Herzl Pl., Suite 101, Beltsville, MD 20705; (301) 937-5677.

Content: A short course on the principles and practice of radiofrequency, microwave, and ultrasound hyperthermia in the treatment of cancer. The course is designed for physicians, medical physicists, engineers, and medical administrators who are involved or intend to be involved in ultrasound, radiofrequency, and microwave thermotherapy in the treatment of cancer. The course will be taught by Dr. Augustine Y. Cheung. The text to be used is "Physical Aspects of Hyperthermia", AAPM Monograph 8, G. Nussbaum, ed., American Institute of Physics, NY, 1983.

SHORT COURSE: NON-IONIZING RADIATIONS: BIOPHYSICAL AND BIOLOGICAL BASIS, APPLICATIONS AND HAZARDS IN MEDICINE AND INDUSTRY.

Date: August 8-12, 1983

Place: Cambridge, MA

Fee: \$850

Requests for Information: Dir. of Summer Sessions, Room E19-356, MIT, Cambridge, MA 02139

Content: Topics covered include lasers, microwaves, ultraviolet radiation, magnetic fields, and ultrasound. A detailed reading list and other pertinent materials will be provided. Practical demonstrations will be given of the instruments and techniques used for measurement of the intensity level of each form of energy for implementation of safety programs in the workplace. The discussion on microwaves will include physical characteristics and field measurement, dosimetry, electrical properties of biological tissues in constant and varying fields, absorption, thermal effects, non-thermal effects; results and mechanisms in blood, eye, testes, malignant tumors, growth; applications in diathermy, and in cancer therapy; health hazards of radar, microwave ovens, industrial RF heaters and sealers, Eastern and Western safety standards and their biophysical basis. The discussion on magnetic fields will include geomagnetic environment, static and varying magnetic fields, biological effects; potential hazards and safety in NMR imaging. The course will be taught by Padmakar P. Lele, M.D., Ph.D., Professor of Experimental Medicine, Department of Mechanical Engineering, Harvard-MIT Division of Health Science Technology. Guest faculty include J. J. Galli, Food & Drug Administration, W. P. Hansen, Ph.D. Ortho Diagnostic Systems, J. L.

Jones, MIT, and M. A. Pathak, Ph.D., Harvard Medical School.

EIGHTH ANNUAL CONFERENCE OF THE AUSTRALIAN RADIATION PROTECTION SOCIETY

Date: August 15-17, 1983

Place: Adelaide, Australia

Requests for Information: Mrs. J. Fitch, Convenor, 1983 ARPS Conference, Private Bag 97, Glenside, SA 5065, Australia

SHORT COURSE ENGINEERING TECHNIQUES FOR CLINICAL HY. TERMIA

Date: August 29-31, 1983

Place: Washington, DC 20052

Requests for Information: Continuing Engineering Education Program, George Washington University, (800)424-9773

Fee: \$685

TECHNIQUES IN STUDIES OF BIOLOGICAL EFFECTS OF LOW-LEVEL MILLIMETER WAVES

Date: September 4-6, 1983

Place: Hotel Alba, Herrsching am Ammersee, West Germany (near Munich)

Sponsor: URSI Commission A "Working Group" on Measurements Related to the Interaction of Electromagnetic Fields with Biological Systems"; cosponsored by the Bioelectromagnetics Society, Gesellschaft fur Strahlen- und Umweltforschung, and the Max-Planck-Institut fur Festkorperforschung
Requests for Information: Dr. Fritz Keilmann, Symposium Chairman, Max-Planck-Institut fur Festkorperforschung, 7000 Stuttgart 80, Germany; Tel.: (0711) 6860/603 or 6860/651; Telex: 7-255 555.

Subject Matter: The symposium will provide a discussion platform for scientists studying biological effects of low-intensity millimeter microwave radiation. Emphasis will be on experimental approaches and on experimental details. Specific goals are: (i) which biological systems (which biological endpoints) may be of use, and which requirements do they impose on the microwave system, and (ii) which irradiation configurations may be of use, and how can the microwave fields as well as the microwave-induced temperature fields be controlled.

Language: English

Estimated Attendance: 40

Symposium Publications: No publications of proceedings; main results of the symposium will probably be summarized in the form of a detailed report for

Meetings and Conferences

Biological Effects of Nonionizing Electromagnetic Radiation VII(2-4), July 1983

publication in a journal like Bioelectromagnetics.

FIFTH EUROPEAN CONGRESS ON RADIOLOGY

Date: September 5-10, 1983

Place: Bordeaux, France

Requests for Information: Mme. N. Hargous, Hospital Pellegrin, Service de Radiologie, Place Amelie Rabaleon, F-33076, Bordeaux, France

36TH ANNUAL CONFERENCE ON ENGINEERING IN BIOLOGY AND MEDICINE

Date: September 12-14, 1983

Place: Hyatt Regency Hotel, Columbus, OH

Sponsor: Alliance for Engineering in Medicine and Biology, 4405 East-West Highway, Suite 210, Bethesda, MD 20814; 301/657-4142

Requests for Information: Mrs. P. I. Horner, AEMB; Conference Chairman is Prof. Herman R. Weed, The Ohio State University; Program Chairman is Baxter Womack, Ph.D., University of Texas
Content: In addition to the traditional topic areas, special sessions will include the following categories: Instrumentation; Bioelectric Phenomena; Medical Imaging; and Standards & Regulations. The deadline for receipt of abstracts is April 15, 1983. Short courses will be held 11 September 1983.

THIRD ANNUAL MEETING OF THE BIOELECTRICAL REPAIR AND GROWTH SOCIETY

Date: October 2-5, 1983

Place: Gateway Holiday Inn, San Francisco, CA

Requests for Information: Executive Secretary, BRAGS, 425 Medical Education Bldg., 36th and Hamilton Walk, Philadelphia, PA 19104; (215) 898-8653

SHORT COURSE

CURRENT ISSUES AND TRENDS IN CONTROLLING OCCUPATIONAL EXPOSURES TO RF/MICROWAVE RADIATION

Date: October 11-13, 1983

Place: Salt Lake City, UT

Requests for Information: K. Blosch, Rocky Mountain Center for Occupational and Environmental Health, Univ. of Utah, Salt Lake City, UT 84112; (801) 581-5710

5th COURSE BIOLOGICAL EFFECTS AND DOSIMETRY OF NON-IONIZING RADIATION: STATIC AND ELF ELECTROMAGNETIC FIELDS

Date: November 15-25, 1983

Place: Erice, Italy

Requests for Information: Persons from Europe wishing to attend the course should write to Professor Martino Grandolfo, Istituto Superiore di Sanita, Viale Regina Elena 299, 00161 Rome, Italy; persons from other continents should write to Professor Sol M. Michaelson, The University of Rochester, Medical Center, 601 Elmwood Avenue, Rochester, NY 14642. Closing date for application is September 15, 1983

Fee: \$500 (covers full board and lodging)

Content: Part of the course will be devoted to studies, both of a theoretical and experimental nature, relating to potential mechanisms of interaction of static and ELF electromagnetic fields with biological systems. After a detailed review of the fundamentals of physics and biology connected with the interaction of these fields with living matter, the lectures will provide an updating of the techniques developed for the detection and the dosimetry of these energies and a critical analysis of their biological effects in relation to the establishment of safety standards.

SIXTH INTERNATIONAL CONGRESS OF THE RADIATION PROTECTION ASSOCIATION

Date: May 7-12, 1984

Place: International Congress Center, Berlin, Germany (DFR)

Sponsor: Int. Radiation Protection Assn. (IRPA)
Requests for Information: R. Neider, Sec General, Bundesanstalt fur Material Prufung, Unter Den Eichen, 87, D-1000 Berlin 45, Germany (DFR)

Content: The scientific sessions of the congress and the exhibit cover all aspects of radiation protection from basic research to practical applications with special emphasis on the risk assessment from ionizing and non-ionizing radiation as compared to risks derived from all other man-made sources (400 papers in English, French, and German)

BIOELECTROMAGNETICS SOCIETY SIXTH ANNUAL MEETING

Date: July 12-17, 1984

Place: Omni Hotel, Atlanta, GA

Sponsor: Bioelectromagnetics Society

Requests for Information: BEMS Headquarters, 1 Bank Street, Gaithersburg, MD 20878; 301/948-5530

EIGHTH INTERNATIONAL BIOPHYSICS CONGRESS

Date: July 19 - August 4, 1984
Place: Bristol, United Kingdom
Sponsor: Int. Union of Pure & Applied Biophysics
Requests for Information: Dr. H. C. Watson, Dept.
of Biochemistry, The University, Bristol BS8 1TD,
United Kingdom

Requests for Information: Contact Professor Saul
Rosenthal, Polytechnic Institute of New York, Route
110, Farmingdale, NY 11735

Note: A joint meeting with the Bioelectromagnetics
Society is tentatively scheduled for August 27-30.

URSI SYMPOSIUM

Date: August 29 - September 7, 1984
Place: Florence, Italy
Sponsor: URSI

MEETING OF THE EUROPEAN SOCIETY FOR
THERAPEUTIC RADIOLGY AND ONCOLOGY

Date: September 9-15, 1984
Place: Jerusalem Hilton, Jerusalem, Israel
Sponsor: KENES
Requests for Information: Prof. Z. Fuks, Head,
Dept. of Radiation and Oncology, Hadassah Medical
Center, Jerusalem, Israel

CURRENT RESEARCH

TRANSLATIONS FROM FOREIGN LITERATURE

From time to time, Information Ventures, Inc. will prepare full-text translations of foreign research efforts on the biological effects of nonionizing electromagnetic fields for publication in this Digest. The first of these translations is presented below. We welcome your comments and suggestions for future translations.

EFFECT OF MILLIMETER-BAND ELECTROMAGNETIC RADIATION ON BACTERIAL CELLS. (Rus.) A. Z. Smolianskaia. In: Non-Thermal Effects of Millimeter-Band Radiation, N. D. Deviatkov, Editor, published by the USSR Academy of Science, Institute of Radioengineering & Electronics, Research Council on a Problem of "Physical Electronics", Moscow, pp. 132-146, 1981.

Development of millimeter-band generators of the backward-wave-tube type created a natural interest in the biological effects of this type of electromagnetic radiation. From the early 1960's, under the leadership of academician N. D. Deviatkov (1), a number of organizations started to study the effects of this radiation on biological materials and initially on bacterial cells.

Initial interest was associated primarily with an antimicrobial effect. This effect, during the interaction of an electromagnetic field with biological materials, can be caused by either thermal action or by the specific action of radiation on the structure. The specific effect is of greatest interest. Various researchers (2,3) showed that the use of low-intensity radiation that did not cause heating of bacterial cells produced the lethal effect. In addition, it was shown that after exposure to low-intensity radiation in the 6.3-6.9-mm range, some of these waves had an antibacterial effect while others had not.

The data on the antibacterial effect of millimeter-band radiation of nonthermal intensity were used as a basis for the study of the effects of these waves on bacterial systems responsible for lethal synthesis (4). The first experiments with induction of lethal synthesis of colicin in *Escherichia coli* K12 C 600 (*E_k*) produced interesting results. Irradiation of this strain with waves in the 5.8-7.1-mm range indicated various interesting characteristics of the interaction of millimeter-band waves with bacterial cells. Firstly, these experiments showed the existence of active and inactive wavelengths, i.e. wavelengths which increase the number of colicin-synthesizing cells and wavelengths which do not. A detailed analysis of 11 neighboring wavelengths with the aid of a special wavemeter capable of measuring wavelengths with a resolution of 0.01% was conducted. The curve obtained (Fig. 1) indicated the markedly resonant type of relationship between the number of colicin-synthesizing bacteria and the wavelength. The resonant type of the effect was confirmed later after irradiation of numerous bacterial and mammalian cells. It should also be men-

tioned that the system showed a high sensitivity to the wavelength: a shift of 0.02 mm resulted in the disappearance of the effect (5).

Secondly, the effect was directly related to the duration of irradiation: maximum effect was observed after 2-hr irradiation; the effect was significantly lower after irradiation for 1 hr, while 30-min irradiation failed to produce the effect.

And, thirdly, the effect was relatively independent of the radiation power within a wide range. After reaching a threshold power of 0.01 mW/cm², a 100-fold change in the power flux density (from 0.01 mW/cm² to 1 mW/cm²) did not affect significantly the biological effect (Fig. 2).

The data obtained in the experiments with colicogenic bacteria were of paramount importance since they indicated that the lethal effect of millimeter band electromagnetic radiation of nonthermal intensity can be caused not by direct action of the energy of this radiation which is too low to produce such effects (see below), but rather by the indirect action due to resonant stimulation of the bacterial systems and mechanisms of lethal synthesis.

This conclusion was confirmed in a study of the effects of similar radiation on the lysogenic strain of *Staphylococcus aureus* No. 962. In our laboratory, A. V. Suslov showed that irradiation with 6.55-mm electromagnetic waves (45.79 GHz) resulted in a 2.2 fold increase in the synthesis of phage particles lethal for the host cell. The critical effect with respect to wavelength was 0.005 mm (Fig. 3).

These findings thus indicated that the induced genetic systems which regulate lethal synthesis in bacteria, are sensitive to certain wavelengths in the millimeter range and that this effect is of a markedly resonant nature.

The observed characteristics of the effect of millimeter-band electromagnetic radiation of nonthermal intensity on functional activity of genetic systems of bacteria cells shed, in our opinion, some light on the multiplicity of effects of millimeter-band waves on various metabolic processes in bacteria detected by various researchers. It was shown, for example, that certain millimeter-band waves change protein metabolism in bacteria (7,8). In other experiments, 6-7-mm waves increased the yield of thrombolytic proteases in *Aspergillus* and in *Nocardia* (9,10). The same researchers have found that changes in wavelength and number of irradiations causes changes in functional activity of various systems of bacterial cells producing either caseinolysine or flarinolysine. The researchers from the Leningrad Institute of Antibiotics and Enzymes have found changes in the enzymatic activity of *Basidiomycetes* after exposure to millimeter-band waves (11). We have studied the effects of millimeter-band waves on beta-lactamase (penicillase) synthesis in penicillin-resistant strains of *Staphylococcus aureus* and *Escherichia coli*. It was found



that certain wavelengths (6.468 and 6.478 mm) inhibited the inducible enzyme synthesis in *Staph. aureus* and did not affect the constitutive enzyme synthesis in *E. coli*. It is important to note that irradiation did not affect penicillase activity. This phenomenon was verified in experiments with irradiation of exogenous enzyme. The relationship between inhibition of enzyme synthesis and wavelength was of a markedly resonant type: a $\pm 0.005\text{-mm}$ change in wavelength resulted in a disappearance of the effect (Fig. 3). Another interesting detail was observed in this system: a tenfold decrease in bacterial multiplicity resulted in a fourfold increase in the effect. Since a characteristic morphological feature of a staphylococcal colony is grape-like clustering, the observed data may indicate a shielding effect.

Comparing these data with the results obtained after exposure of colicinogenic strain of *E. coli* and lysogenic *Staphylococci* indicated that the most probable application site of millimeter-band radiation energy was the repressor system that blocked the induction of certain metabolic cycles. Since the inducible metabolic processes are widely spread among the living organisms, the possibilities of electromagnetic field effects are also diversified (12).

The observed effects of millimeter-band radiation on enzymatic systems of bacteria can lead to changes in cell division. Webb and Booth (13) studied the effects of millimeter waves in the 4.68-3.94-mm range on division of *Escherichia coli* 3_R cells. Radiation of wavelength 4.41-mm stimulated cell division, while 4.54-mm, 4.19-mm, and 4.11-mm waves inhibited cell division. It was found that radiation of wavelength 4.54-mm inhibited assimilation of amino acids and thiamine by *Escherichia coli* cells. Waves of wavelength 4.22-mm caused a significant decrease in accumulation of all labeled metabolites, the 4.19-mm waves caused slight decrease in thiamine and amino acid accumulation, and 4.11-mm waves corresponded to the maximum of protein accumulation. All these waves inhibited cell division. Irradiation of this strain with 4.41-mm waves increased accumulation of ¹⁴C-uracil and of amino acids and enhanced cell proliferation. It should be mentioned that thiamine assimilation remained unchanged and this can and does lead to the appearance of morphologically altered variants.

The changes in growth rate and appearance of morphological variants after exposure of bacteria to millimeter-band radiation were observed in numerous studies. V. F. Kondrat'eva et al (14) showed the changes in morphology of colonies and cells as well as the changes in biological properties (spore formation, saccharolytic, proteolytic and antigenic properties, pathogenicity) of a number of anaerobic (*Clostridium*) and aerobic (*Proteus*) bacteria after irradiation with 7.2-mm waves. Changes in the morphology of bacterial cells were also noted by other researchers (6). The most frequent morphological changes after exposure to millimeter-band electromagnetic radiation were observed in fungi. These changes occurred in *Saccharomyces cerevisiae*

pil⁻¹ after irradiation with a wavelength of 5.0 mm and a power flux density of 0.25 MW/cm². Similar changes were observed after irradiation of *Aspergillus avam* and *Endomycopsis fibuliger*. In the latter case, the authors noted certain changes in biochemical properties of the culture (9,10). Direct observations of the culture growth in a specially designed microscope attached to a generator of millimeter waves showed changes in the intensity of replication of *Rodotorula rubra* (15).

Attempts to induce bacterial mutations by means of millimeter-band radiation failed. We could not find convincing data in the available literature, although various researchers tried to obtain the vaccine strains. But they admitted that the millimeter-band radiation induced very short-term loss of virulence. In certain cases the loss of virulence could be explained by selection of pre-existing variants, since in addition to irradiation, the strains were subjected to culturing.

Thus, the results of experiments conducted by different researchers on different microorganisms indicated the presence of biological activity of millimeter-band electromagnetic fields of nonthermal intensity. The type of wavelength-effect curves and relative independence from the intensity of radiation after reaching a certain threshold value were indicative of the markedly resonant nature of the effect.

The resonant type of response observed in the inducible bacteria explained and confirmed the data obtained in other biological materials. Simple and isolated bacterial cells are an extremely valuable test system for the study of biological effects of millimeter-band electromagnetic fields of non-thermal intensity. The clear-cut data obtained during the study of the effects of this type of radiation on the extrachromosomal, and therefore on relatively autonomic, inducible bacterial systems (colicinogenic factor, temperate phage, penicillase gene) provide a basis for certain generalizations and theoretical models of the mechanisms of this phenomenon.

It is known that ultraviolet radiation with a wavelength of approximately 22,550 Å and energy of approximately 4.9 ev is the most effective inducer of colicin synthesis or of prophage release. It is also known that this is the energy of the same order of magnitude as the energy of C-N, C-C and C=C bonds in protein and nucleic acid molecules (2.1 ev, 2.5 ev, and 4.4 ev, respectively). It is also known that photons with energies of 4-6 ev are selectively absorbed by proteins and nucleic acids. This phenomenon probably causes the biological effects of ultraviolet radiation. Ultraviolet radiation can lead to excitation of valent electrons in atoms, i.e., to be conducive to their jump into higher energy levels. The molecules with excited electrons enter readily into photochemical reactions. These reactions can cause various biological effects: changes in the genetic code (mutations), breaks and subsequent repair of DNA and RNA

molecules, which in turn lead to excitation (in case of repressor damage) or inhibition of functional activity of various genetic systems.

But the energy of a millimeter-band electromagnetic field is significantly lower than that of ultraviolet radiation.

It is known that $E = h\nu = hc/l$, where
 $h = 6.62 \times 10^{-34}$ erg·sec
 $c = 3 \times 10^{10}$ cm/sec
 $l = 6.5 \times 10^{-1}$ cm or 7.1 mm.

Therefore,
 $E = (6.62 \times 10^{-34}) \cdot (3 \times 10^{10}) / 6.5 \times 10^{-1}$
= 3.06×10^{-16} erg = 1.9×10^{-4} ev,
since 1 ev = 1.60×10^{-12} erg.

Therefore, the energy of the millimeter-band electromagnetic field is approximately 10^4 times lower than the energy of chemical bonds in biological molecules. Energy of this order of magnitude can only cause intramolecular oscillations or rotation of the entire molecule. This was shown by L. G. Koreneva and V. I. Gaiduk (16) for histidine in the hemoglobin molecule. But if these oscillations resonate with the intrinsic oscillations of intracellular molecules, the resultant effect can be equal to that observed after exposure to such powerful agents as ultraviolet radiation or chemical agents, which damage the DNA structure and induce various biological processes. It is possible that the absence of a mutagenic effect from millimeter-band radiation is due to the absence of direct damage to the DNA molecule.

A. M. Makhov (17) calculated the power of electromagnetic radiation required for the resonant effect on one cell of *Staphylococcus aureus* to inhibit the inducible penicillase synthesis. Stabilization of the effect was achieved with power of approximately 7×10^{-6} W/cm² for 1-micron medium layer and 5×10^{-14} W for a single cell. Since the energy of a quantum of electromagnetic radiation is equal to 10^{-4} ev, then the number of quanta per one cell per 1 sec under the condition of saturation of the biological effect is approximately equal to 5×10^9 . The relaxation time for the resonating cell structures at a given power flux density can vary from 2×10^{-10} to 2×10^{-7} sec, depending upon the resonating structure. Therefore, the resonant absorption of the millimeter-band electromagnetic field can cause changes in the activity of various functional cell systems. These results showed good agreement with the data on the effects of electromagnetic fields of the same frequency on induction of colicin synthesis. This can indicate the similar mechanism of resonant interactions in different biological systems.

The present communication summarizes the results of experiments of Soviet scientists who initiated the studies of the effects of millimeter-band radiation on bacterial cells.

In recent years, intensive studies of the effects of millimeter-band radiation have been conducted

abroad.

In 1977, Grundler, Keilman and Frohlich (18) showed a resonant change in the growth rate of yeasts which increased or decreased depending upon the frequency of radiation (approximately 42 GHz) after irradiation with VHF fields at a power of several MW/cm². Careful regulation of temperature conditions excluded the trivial thermal effect of radiation. Next year, Grundler and Frohlich (19) confirmed the independence of the effect from temperature and showed that the critical frequency was 0.01 GHz. In 1977, Webb, Stoneham and Fronlich (20) studying the Raman spectra of actively replicating synchronous *E. coli* culture showed that the excitation levels of spectra of a markedly resonant type corresponded to the metabolic cycles of bacterial cells. These data indicated a relationship between coherent millimeter waves and biological effects.

Italian researchers Dardanoni, Torregrosso, et al. (21) showed that irradiation with UHF waves pulse-modulated at 72 GHz reduced the viability of cellular suspension of *Candida albicans*, while irradiation with continuous waves failed to produce such an effect.

A group of U.S. researchers (22) observed an effect similar to that detected in our experiments after irradiating for 1-hr cells of the colicinogenic strain of *E. coli* containing colicinogenic factor EI. Maximum induction of colicin synthesis was observed after irradiation at a wavelength of 5.8 mm and a power flux density of 0.5 MW/cm². Similar data on induction of colicin synthesis were obtained by other researchers.

French scientists Dardalhon, Averbeck and Bertheaud (23) showed that millimeter-band radiation can affect the growth rate of bacteria. The effect depended upon the frequency of radiation. The radiation did not cause damage to cellular DNA. These researchers did not observe nuclear-chromosome mutations (experiments with DNA repair-deficient bacteria) or cytoplasmic mutations (in mitochondrial DNA from diploid yeasts). This confirms our opinion that the basic mechanism of the effect of millimeter-band radiation is not associated with gross damage to DNA structure but rather with changes in configuration of the functional molecule without breakage of intramolecular bonds but with changes in functional activity. In addition, these authors have found that the increase in the number of zygotes between two haploid yeast strains was achieved only after irradiation for at least 330 min at a frequency of 70.5 GHz, a power flux density of at least 60 MW/cm², and a distance from the horn to the culture of 2 mm (at a distance of even 10 mm, the effect could not be observed). Comparing this effect with the effects observed after the heating indicated that it corresponded to the heating from 20 C to 23 C. Therefore, irradiation at these parameters was equivalent to heating by 3 C. These results confirmed our data and the data obtained by Grundler and Keilman indicating that induction of

colicin synthesis, release of phage, inhibition of beta-lactamase synthesis and bacterial cell growth required significantly higher temperatures (approximately 40°C). Such increase in temperature can not be achieved at powers lower than 1 MW/cm².

Since the effect of millimeter-band waves is associated with the resonant response of the biological system, its detection required a large number of coincidences. It was necessary that the wave hit a cell, that the cell was in an appropriate stage of development, that the wave hit the cellular structures which could resonate with the given wavelength, and finally, that the irradiated population contained a sufficient number of cells meeting all these requirements.

In our opinion, this determines the multiplicity of the effects observed by one and the same authors. For example, Athey and Krop (24) initially observed induction of colicin synthesis in *Escherichia coli* 3110 Col EI after irradiation with millimeter-band radiation. But in subsequent experiments, all attempts to induce prophage in lysogenic strain of *Escherichia coli* BR-475 (l, lac⁺) failed. In the latter case, the authors tried to detect production of a free phage not by a conventional plaque method, but rather colorimetrically by lactamase production (in the test strain, lac⁺ gene transcribed together with l gene). Since these authors did not observe the radiation-induced increase in the enzyme yield, they doubted the possibility not only of prophage induction but also of induction of colicin synthesis. They argued that induction of temperate phage and of col factor have similar mechanisms. This statement can not be accepted for several reasons. Firstly, the similarity of the mechanism of induction of temperate phage and that of col factor is quite relative and is limited to observations that such inducers as ultraviolet rays, nalidixic acid, mitomycin C, etc., induce both temperate phage and colicin synthesis. But we have reason to believe that in contrast with the abovementioned inducers, the mechanism of the effect of millimeter-band radiation is not associated with damage to the DNA molecule.

Secondly, the similarity of derepressors does not mean a similarity in the structure of repressor molecules, which play an important role in response to the effect of millimeter-band radiation. At present we have some data on the protein nature, molecular weight and some other parameters of phage repressor, but nothing is known about the repressor of col factor.

And, thirdly, the detection of similar effects and especially the denial of their existence requires similar experimental conditions. It is especially true for studies of the effects of millimeter-band radiation. In our experiments on the effects of millimeter-band UHF-radiation on bacterial cells we encountered various manifestations of the effect: acceleration and inhibition of the growth rate, potentiation and inhibition of the functional activity of different organelles in bacterial cells, and

lethal and modification effects. We observed, for example, a situation in which the inducible system of col factor EI in *E. coli* responded by an increase in colicin synthesis, while the inducible synthesis of beta-galactosidase in *Staphylococcus aureus* was inhibited. But in both cases, the genes regulating these syntheses were localized in the plasmids and showed similar response to such inducers as ultraviolet rays and mitomycin C. In the case of *Staphylococcus aureus* containing the temperate phage, the release of free phage after irradiation with a millimeter-band field could be observed in a very narrow wavelength range.

Therefore, we believe that the development of millimeter-band generators provided us with a tool for analysis of fine biological processes on a molecular level. But the mechanism of these interactions still requires a detailed analysis.

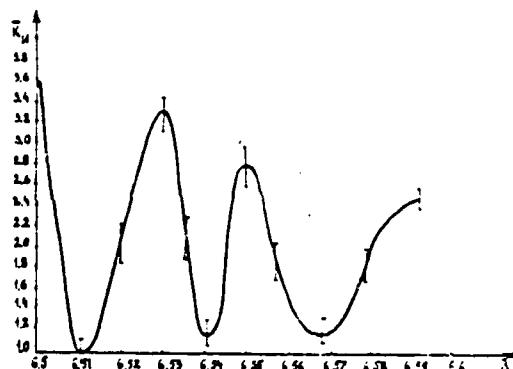


FIGURE 1

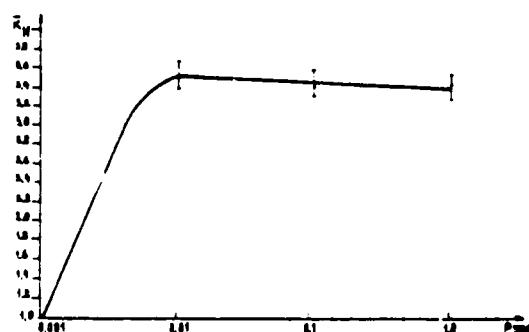


FIGURE 2

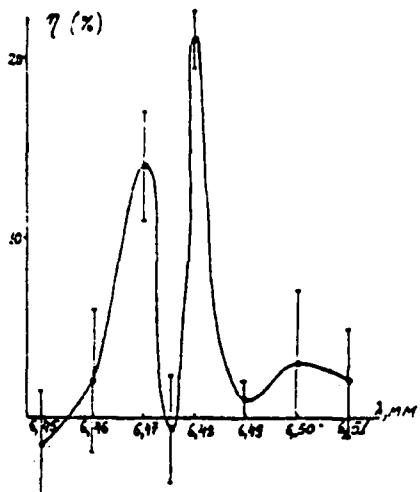


FIGURE 3

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FOR OUR NEXT ISSUE

BIOLOGICAL EFFECTS OF MICROWAVE RADIATION. (Hung.)
Almassy, Gy.; Szabo, L.; and Ballai, L. *TKI* 27
(1-2):15-45, 1982.

In this paper, the main biological effects of microwaves are surveyed, medical applications are outlined, and the draft of a new Hungarian standard on protection against radiation is presented.

NON-IONIZING RADIATION: HEALTH AND SAFETY ISSUES IN THE 98TH CONGRESS. Dodge, C. H. and Kainz, R.; Library of Congress, Congressional Research Service Major Issues System, May 9, 1983.
(The following is excerpted from the above source.)

ISSUE DEFINITION

New technologies and advancements in the electronics, communication, and other industrial and scientific fields have provided many benefits to society. The development of these technologies has also resulted in an increased exposure of the general population to low-level non-ionizing radiations.

This mini issue brief provides a short background on non-ionizing radiation, identifies the common sources of low-level non-ionizing radiations and summarizes available information on the known human health effects associated with non-ionizing radiation exposures.

The effects on human health from these low-level exposures are not well understood. In the 96th and 97th Congresses, two hearings were held on health issues related to occupational exposure to microwave and radiofrequency radiations. Concerns persist in the 98th Congress about the possible health effects of chronic exposure on non-occupational populations to very low-level RF/MW radiations and low-level electric and magnetic fields near power lines. The fact that there remain no formal standards for either occupational or non-occupational exposure to RF/MW radiations is of continuing congressional concern. Currently, there is concern in committees of the House and Senate with oversight authority over the EPA that the Administration has proposed zeroing out the EPA's Health Effects Research Laboratory (HERL) in Research Triangle Park, North Carolina. That laboratory houses the largest non-defense Federal research program on the biological effects of non-ionizing radiations.

Sources of Microwave and Radio-frequency Radiations

Microwave and radio-frequency radiation sources have continued to come closer to major population centers. These sources include a) communication sites; b) navigation devices; c) medical diathermy units; d) food ovens; e) commercial radio; f) television broadcast stations; g) generators; and h) Citizen Band (CB) radios. The Task Force on Research Planning in Environmental Health Sciences has concluded that these microwave sources are responsible for an estimated half of the U.S. population living in some measureable microwave environment. The level of exposure reported by the Task Force is far below the recommended safe level of exposure (10 mW/cm^2) for most normal circumstances. The most rapidly increasing source of public exposure to RF radiation has been the CB radio. The hazard associated with the CB radio is due to the close proximity of the antennas to the individual.

Potential Health Effects of RF and MW Radiation

At sufficiently high levels of field intensity, the effects of RF/MW radiation are thermal in nature. The denaturation or "cooking" of biomolecules can be induced only at field intensities that are so high the temperature of the target tissue is significantly increased. Thus the absorption of MW field intensities on the order of 100 mW/cm^2 results in rapid tissue heating. If the exposure is long enough, there is irreversible tissue damage.

In humans, the two organs at greatest risk of RF/MW injury are the eye and testicle, because of their inability to dissipate heat via circulatory system mechanisms. Accordingly, chronic exposure to high intensities of RF/MW radiation can result in male sex cell destruction and thermally-induced cataracts. At very high intensities of RF/MW radiation (i.e., greater than 100 mW/cm^2) skin burns can be induced. However, such burns are reversible in nature.

Epidemiological studies of human populations in the Soviet Union, Czechoslovakia, Poland, and Sweden exposed occupationally to low-level RF/MW radiation (i.e., below 1 mW/cm^2) have yielded indications of changes in human nervous system and cardiovascular function after prolonged exposure (one year or more), but these may be reversibly altered. A number of behavioral changes have also been reported. These studies are subject to controversy in this country because no comparable data exists for similarly exposed occupational populations.

At present, the major unanswered question is whether there are other mechanisms of interaction between RF/MW radiation and biological systems that can cause reversible or irreversible alterations at field intensities, but that do not result in detectable tissue heating (i.e., below 10 mW/cm^2).

Microwave and Radiofrequency Radiation Standards

Exposure standards for microwave and radiofrequency radiation are usually expressed in terms of the rate at which energy flows through the human body. This rate is called power density and is commonly expressed in units of milliwatts or microwatts per square centimeter.

Title 21, Chapter 1, Subchapter J of the Code of Federal Regulations defines the power density limit for microwave ovens. Ovens shall not exceed 1 mW/cm^2 exposure at the oven surface prior to sale or initial use. Those ovens which are in active use can not exceed an exposure limit of 5 mW/cm^2 .

In 1971, OSHA adopted the 1966 version of the American National Standards Institute (ANSI), C95.4 Committee, 10 mW/cm^2 exposure standard for workers. More recently, ANSI has proposed a reduction of this standard to 1 mW/cm^2 for the frequency range between 30 and 300 MHz. A new OSHA criteria document on occupational microwave and radiofrequency

radiation exposure may be issued in the near future. Currently, the EPA has announced plans to issue guidance to other Federal agencies to limit exposure of the general public to radiotfrequency radiation (*Federal Register* 47(247):57338-57340, December 23, 1982). The EPA guidance will not address occupational exposure or classes of microwave and radiofrequency sources that can best be controlled by existing performance standards.

Of congressional concern is the fact that the U.S. remains the only country for which there is no formal occupational exposure standard for RF/MW radiation. Occupational exposure standards in most Western countries, which range from 1 mW/cm² to 10 mW/cm², limit the amount of heat generated when radiation is absorbed in human tissue. Most of these standards do not contain special provisions for exposure of the public. However, Canada has proposed to limit exposure of the public to one-tenth of its occupational exposure limit of 10 mW/cm².

In 1979, the Federal Communications Commission (FCC) came out with a Notice of Inquiry (NOI) into possible health hazards of RF at FCC facilities (FR vol. 44, p. 37008, June 25, 1979). Responses to the NOI culminated in a Notice of Proposed Rule Making (NPRM), in 1982 (FR vol. 47, p. 8214, Feb. 25, 1982; FR vol. 47, p. 10871, March 12, 1982; FR vol. 47, p. 27384, June 24, 1982). The NPRM allows FCC to assess possible RF hazards at new FCC facilities. Existing FCC facilities are exempt. There is no standard associated with the NPRM.

The countries of Eastern Europe, including the USSR, Poland, and Czechoslovakia have lower exposure standards for most occupational situations, for example, 0.01 mW/cm² for microwave frequencies. Exposure standards for the public at these frequencies are even lower (i.e., 0.005 mW/cm² in the USSR). These standards are based on behavioral and clinical studies that have not been repeatable or replicable in the West. Many U.S. experts question the validity of these studies and standards and whether and to what extent the standards are actually enforced.

HEARINGS

U.S. Congress. House. Committee on Science and Technology. Subcommittee on Investigations and Oversight. Potential Health Effects of Video Display Terminals and Radiotfrequency Heaters and Sealers. Hearings, 97th Cong., 1st Sess. May 12-13, 1981; Washington DC. U.S. Govt. Printing Office No. 13, 764 p., 1981.

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50-60 Hz ISSUES: CONGRESSIONAL PERSPECTIVE.

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The Issue

Sharply increased congressional concern about the significance of reports listed in Tables 1 and 2 reporting increased incidence of cancers in certain public and occupational populations exposed to weak 50-60 Hz electric and magnetic fields.

Questions Addressed in 50 Hz, Power Frequency, and COMAR Workshops

1. How significant are the studies epidemiologically?
2. How should CRS evaluate the studies for the Congress and its constituency?
3. How creditable are the experimentors (is there experimental bias?)
4. Were the studies adequately designed?
 - sufficiently large populations?
 - "control" populations? (what is a control population?)
 - other factors contributing to the effects reported (ionizing radiations; toxic substances in the air, water and food; personal health histories; personal health habits etc.)
 - prospective and retrospective peer review of epidemiological studies (i.e. New York Power Line epidemiological and experimental studies)
 - does recent experimental work in the 0-100 Hz range compliment the epidemiology? (i.e. T-lymphocyte responses to pulsed RF/MW fields; germ cell changes etc.)
5. What posture should the concerned Federal regulatory and research agencies (EPA, DOE, NIH, NAS, US/USSR Working Group etc.) assume in the wake of the epidemiology studies reported in Tables 1 and 2? (i.e. is it time to hit the panic button or should increased funding be provided for additional epidemiological and experimental studies?)
6. In general, where do we go from here?

(Note: Responses regarding the above should be forwarded to C. H. Dodge)

TABLE 1.

PUBLIC EXPOSURE AT 50-60 Hz

| <u>Author</u> | <u>Reported Effect (incidence)</u> |
|------------------------------|--|
| WERTHEIMER AND SLEEPER, 1979 | + LEUKEMIA, NEOPLASMS (children) |
| FULTON ET AL, 1980 | NO CHANGE IN LEUKEMIA INCIDENCE |
| PERRY ET AL, 1981 | + SUICIDES |
| TOMENIUS ET AL, 1982 | + TUMOR CASES (children) |
| WERTHEIMER AND SLEEPER, 1982 | + LEUKEMIA, NEOPLASMS (adults) |

Table 2 is presented on the following page

QUESTIONS AND ANSWERS ABOUT BIOLOGICAL EFFECTS AND POTENTIAL HAZARDS OF RADIOFREQUENCY RADIATION
(Office of Science and Technology Bulletin No. 56)
12 p. July 1982 (3 References)

The Federal Communications Commission (FCC) regulates the use of radiowaves and microwaves for communications. Because of its responsibilities in this area the Commission often receives inquiries concerning potential hazards to human health and safety from radiofrequency (RF) and microwave radiation. In recent years there has been a noticeable increase in public awareness and concern over this issue. Increased publicity about new uses of RF and microwave technology has generated much discussion and speculation concerning the alleged "electromagnetic pollution" of the environment. This short publication is designed to provide information on some of the most commonly asked questions about RF and microwave radiation. Included are responses to the following questions:

- What is Radiofrequency Radiation?
- What is Radiofrequency Radiation Used For?
- What Is Microwave Radiation?
- Are Some Forms Of Radiation More Hazardous Than Others?
- What Biological Effects Can Be Caused By RF Radiation?
- What Are Safe Levels For Exposure To RF and Microwave Radiation?
- How Safe Are Microwave Ovens?
- Is It Safe To Use AN Electronic Cardiac Pacemaker Near An RF Source Such As A Microwave Oven?
- How Safe Is The Radiation Emitted By Radio and Television Broadcasting Towers?
- Is There Any Danger From Microwave Point-To-Point Relay Towers? What About Microwave Dish Antennas Used For Satellite To Ground Communication?
- Is There Any Hazard Associated With Hand-Held Walkie-Talkies?
- Which Federal Agencies Are Responsible For Protecting The Public From Hazardous Levels Of RF Radiation?
- What Is The Role Of The FCC In Controlling Potential RF Hazards?
- Where Can I Go For Help If I Have A Complaint Or Question Regarding A Possible RF Hazard?

TABLE 2.
OCCUPATIONAL EXPOSURE TO E AND H FIELDS OF VARIOUS FREQUENCIES

| <u>Author</u> | <u>Occupation</u> | <u>Relative Field Strength (freq.)</u> | <u>Reported Effect (incidence)</u> |
|--|--------------------------------------|--|--|
| MILHAM, 1979 | ALUMINUM WORKERS | >100 gauss (?) | + LUNG CANCER; LYMPHATIC AND HEMATOPOIETIC CANCER: BENIGN BRAIN TUMORS: EMPHYSEMA |
| U.S. NAVY (Sanguine, Seafarer, ELF) 1970-1980 | MAINTENANCE PERSONNEL; LINE WORKERS | WEAK (50-75 Hz) | + BLOOD TRI-GLYCERIDES |
| MILHAM, 1982 | VARIOUS (electrical workers) | STRONG TO WEAK (60 Hz-various) | + LYMPHATIC AND HEMATOPOIETIC CANCERS (lymphoma); LUNG CANCER |
| WRIGHT ET AL, 1982 | VARIOUS (electrical workers) | WEAK (60 Hz-various) | + LEUKEMIA |
| McDOWALL, 1983 | ELECTRICAL WORKERS | WEAK (50 Hz-various) | + LEUKEMIA |
| COLEMAN, 1983 | ELECTRICAL WORKERS | WEAK (60 Hz-various) | + LEUKEMIA |
| NORDSTROM ET AL, 1983 | SWITCH YARD WORKERS; LINE WORKERS | STRONG TO WEAK (50 Hz-various) | - FREQUENCY OF "NORMAL PREGRANCY"; + FREQUENCY OF CONGENITAL MALFORMATIONS |

CURRENT LITERATURE

0337 MORPHOLOGICAL EFFECT OF ELECTROMAGNETIC STIMULATION ON THE SKELETON OF FETAL OR NEWBORN MICE. (Eng.) Hinsenkamp, M. G. (Service de Chirurgie Orthopedique et de Traumatologie, Hopital Erasme, Brussels Univ., Brussels, Belgium); Rooze, M. A. Acta Orthop Scand 53(S196):39-50; 1982 (25 refs).

Morphological effects of electromagnetic (EM) stimulation on skeletogenesis were studied in Swiss mouse limb buds grown *in vitro*. Developing limb buds from fetal or newborn mice were incubated in a semi-synthetic culture medium and exposed to an EM signal (duration 63 msec, peak amplitude 16 mV, burst width 4.8 msec) generated by Electro-Biology Inc. coils for 4-6 days. Contralateral limbs served as controls. Skeletal staining with red alizarin and alcian blue showed that EM stimulation selectively influenced the metaphyseal area; distal limb parts were most sensitive. Hematoxylin-eosin staining of paraffin-embedded sections revealed a thicker proliferative layer of chondrocytes, better cartilage configuration, and better trabecular alignment in stimulated limbs than in unstimulated controls. Differences between stimulated and control limbs were more pronounced in distal than in proximal limb segments, but the differences were not statistically significant. The results indicate that EM stimulation can influence the structure of the developing skeleton in mouse limb buds grown *in vitro*.

0338 HISTOCHEMICAL MODIFICATIONS INDUCED IN VITRO BY ELECTROMAGNETIC STIMULATION OF GROWING BONE TISSUES. (Eng.) Rooze, M. A. (Laboratoire d'Anatomie et d'Embryologie Humaines, Brussels Univ., Brussels, Belgium); Hinsenkamp, M. G. Acta Orthop Scand 53(S196):51-62; 1982 (3 refs).

Histochemical effects of electromagnetic (EM) stimulation on mucopolysaccharide (MPS) content were investigated in mouse embryo limb buds grown *in vitro* for 4-6 days. Toluidine blue, colloidal iron, and alcian blue (pH 1.0 and 2.5) staining demonstrated that epiphyseal content of carboxylated or sulfated acid MPS was higher in stimulated than in contralateral control limbs. This difference was most pronounced in more distal limb segments, i.e., in the youngest structures. Enzyme analysis showed an increase in beta-glucuronidase activity and a decrease in acid phosphatase activity in stimulated limbs. The enzyme differences suggested that EM stimulation induces cellular changes that modify matrix acid MPS content, possibly by affecting membrane permeability or the biochemical mechanism of transmembrane transfer.

0339 TREATMENT OF NON-UNIONS BY ELECTROMAGNETIC STIMULATION. (Eng.) Hinsenkamp, M. G. (Service de Chirurgie Orthopedique et de Traumatologie, Hopital Erasme, Brussels Univ., Brussels, Belgium);

Baillon, J. M.; Danis, A.; de Marneffe, R.; Dozinel, R.; Tondeur, G. Acta Orthop Scand 53(S196):63-79; 1982 (20 refs).

Results of electromagnetic treatment of six non-unions are reported. Home treatment was performed for 12-15 hr/day for 3.5 to 12 mo to sites (2 tibia, 2 femur, 1 humerus, and 1 scaphoid) in which non-union had been present for 12 to 66 mo. Mean length of treatment was 6 mo. The patients (5 male, 1 female, 21-56 yr old) had undergone 1 to 3 operations before treatment; in 3/6 cases, spongeous bone grafts were carried out. None of the patients had undergone surgery within 7 mo prior to the beginning of electric stimulation by Electro-Biology Inc. apparatus. Characteristics of the electromagnetic signal were 5 msec width; 13.5 mV amplitude; and 66 msec period (15 Hz). Radiologic evaluation during treatment revealed softening of non-union sclerotic edges followed by increasing fuzziness in the non-union line and formation of trabecular bone bridges. In two atrophic and two hypertrophic non-unions, clinical progress was faster than radiological healing. Clinical results suggest that electromagnetic treatment is indicated for patients who have undergone several unsuccessful surgical procedures or patients for whom surgery is contraindicated.

0340 RESULTS OF NON-UNIONS TREATMENT BY PULSED ELECTROMAGNETIC FIELD STIMULATION. (Eng.) Sedel, L. (Service de Chirurgie Orthopedique, Hopital Saint-Louis, 40, rue Bichat, 75010 Paris, France); Christel, P.; Duriez, J.; Duriez, R.; Evrard, J.; Ficat, C.; Cauchoux, J.; Witvoet, J. Acta Orthop Scand 53(S196):81-91; 1982 (6 refs).

Bone non-unions in 39 patients (10 females and 29 males, 7-81 yr old) were treated with pulsed electromagnetic fields delivered through Helmholtz coils (Electro Biology Inc. apparatus) placed on each side of the non-union site for 12-14 hr/day for a period of 50 days to 9 mo (average treatment duration, 3 mo). The delays between the initial injury and treatment ranged from 2 mo to 25 yr (mean, 11 mo). The number of previous operations was 0 to 6 (mean, 2). Types of non-union were 17 atrophic, 5 hypertrophic, 4 congenital, and 13 infected. The predominant site was the tibia (20 cases), followed by the femur (11). In 6/37 patients available for follow-up, non-unions did not heal; in 4 of these cases, treatment was applied incorrectly (insufficient immobilization or stimulation for less than a 2 mo period). Healing occurred between 3 mo to 1 yr (mean, 6 mo) in 31/37 patients; 21 unions were strong with a large callus and 10 were weak. The possibility that factors such as surgery within 2 mo of treatment or long-term immobilization may have caused healing in 15/31 unions is considered. However, pulsed electromagnetic field stimulation appears to have played a real role in achieving 16/31 unions.

0341 IMPACT OF LOCALIZED MICROWAVE HYPERTERMIA ON THE OXYGENATION STATUS OF MALIGNANT TUMORS. (Eng.) Otte, J. (Dept. Physiology, Univ. Mainz, D-6500 Mainz, W. Germany); Manz, R.; Thews, G.; Taupel, P. *Adv Exp Med Biol* 157:49-55; 1982 (14 refs).

Oxygenation changes in tumors during hyperthermia induced by microwave (MW) radiation were investigated. DS carcinosarcoma cells implanted in the hind limbs of Sprague-Dawley rats were exposed to localized 2.45 GHz MW heating at 40, 43, or 45 C for 30 min when tumor volumes had reached 1.5-5.0 ml. A cyrophotometric micromethod was used to measure the oxyhemoglobin (HbO_2) saturation of single red blood cells within tumor microvessels. During control conditions (mean tumor tissue temperature of 35 C) the HbO_2 data obtained in tumors were scattered over the whole saturation range. Heating at 40 C resulted in significant improvement of tumor oxygenation, as evidenced by a shift to higher HbO_2 saturation values. In contrast, heating at 43 C resulted in decreasing saturation, and heating at 45 C was followed by a drastic fall in HbO_2 values. No substantial changes were observed in the core temperature of the rats during MW application to the hind foot. Therefore, systemic changes did not mask or enhance alterations in tumor blood flow or tissue oxygenation status. Changes in tumor oxygenation during hyperthermia are apparently mediated through changes in tumor blood flow, which is increased by moderate hyperthermia, but which declines at temperatures higher than +2 C, and ceases almost completely after 45 C. Microcirculation may be affected by heating time as well as by tissue temperature levels. When the heating time was increased from 30 min to 60 min, deterioration of the microcirculation, and thus of the tumor oxygenation, occurred at 40 C.

0342 ADJUVANT HYPERTERMIA IN THE IRRADIATION OF METASTATIC TUMOR MASSES UTILIZING 2450 MHZ MICROWAVES. (Eng.) Fazekas, J. T. (Dept. Radiation Therapy and Nuclear Medicine, Thomas Jefferson Univ. Hosp., Philadelphia, PA 19107); Nerlinger, R. E.; Waterman, F. M.; Leeper, D. B. *Adv Exp Med Biol* 157: 99-107; 1982 (14 refs).

Microwave (MW) hyperthermia was administered adjuvant to modest doses of radiotherapy to study the response obtained among 37 patients with carcinoma (37 adenocarcinoma or squamous), melanoma (21), lymphoma (6), and sarcoma (3). Direct contact (MW) applicators operated at 2450 MHz with a maximum power of 100 W were used to deliver hyperthermia treatment (tumor temperature of 42.5-44.5 C in 6-8 40-50 min heating sessions, 2/wk for 3-3.5 wk) prior to electron beam radiotherapy. Effective hyperthermia conditions (42.5 C or beyond) required 5-10 min at an applied power of 30-50 W depending on blood flow, tumor size, and other physiologic factors. Nonperturbing intralesional Luxtron or Vitek probes were used to monitor tumor tempera-

ture measurements. Thermostatically controlled circulating water was used for surface cooling. Water temperature was maintained at 44 C for tumors with no overlying tissue. To spare the skin while increasing the power output, colder water temperatures were utilized for tumor deposits that were subcutaneous or below. Complete response (CR: absence of all visible and palpable tumor) was seen in 8/15 evaluable melanoma patients, and partial response (PR: 50% or more tumor regression) in 3/15. For carcinomas, CR was observed in 13/48 evaluable patients and PR in 15/48. When tumor response was analyzed by anatomic region, skin overlying chest wall had CR and PR rates of 70% and 60% respectively. It was concluded that 2450 MHz MW hyperthermia is quite effective for tumor deposits of melanoma and carcinoma when tumor thickness does not exceed 2.5 cm; skin cooling by circulating water prevents serious skin complications and aids in improving the therapeutic ratio; previous therapies do not prevent the application of effective combined heat and radiotherapy since no serious late skin effects were seen in these patients.

0343 LOCAL IONIZING RADIATION WITH AND WITHOUT MICROWAVE INDUCED HYPERTERMIA IN SUPERFICIAL MALIGNANT TUMORS IN BRAIN. (Eng.) Lindholm, C. E. (Lund Univ. Hosp., Lund, Sweden); Kjellen, E.; Landberg, T.; Mercke, C.; Nilsson, P.; Persson, B. *Adv Exp Med Biol* 157:145-146; 1982 (no refs).

Patients with superficial brain tumors (less than 7 cm diameter and less than 3 cm deep) were treated with x-rays, electrons, or ^{137}Cs gamma rays (3.00 Gray units in 10 fractions) alone or in combination with 2,450-MHz microwave hyperthermia (42.5-43.5 C for 45 min, 1/wk or 2/wk for 2 wk) delivered by a computerized system using a 90 mm diameter circular direct contact applicator. The automatic control system uses a pulsed irradiation technique and reads tumor and normal tissue temperature via thermistor probes. Results of combined vs single modality treatment were evaluated in four patients with more than one superficial tumor. More rapid and more lasting tumor regression occurred in patients treated with the combined modalities than in patients treated with radiotherapy or hyperthermia alone.

0344 EFFECTS OF WEAK AMPLITUDE-MODULATED MICROWAVE FIELDS ON CALCIUM EFFLUX FROM CAT CEREBRAL CORTEX. (Eng.) Adey, W. R. (Res. Service (151), V.A. Hospital, 11201 Benton Street, Loma Linda CA 92357); Bawin, S. M.; Lawrence, A. F. *Bioelectromagnetics* 3(3):295-307; 1982 (33 refs).

The effects of a sinusoidally modulated microwave field on the efflux of brain calcium ($^{45}\text{Ca}^{2+}$) were studied in awake, intact cats immobilized under local anesthesia. The cats were exposed for 60 min to a

3.0-mW/cm² 450-MHz field in a horn radiator. A 16-Hz sine wave was used to amplitude modulate the signal to a depth of 35% and its output was applied to a broadband linear power amplifier with a maximum output of 80 W. Tissue dosimetry showed a field of 33 V/m in the interhemispheric fissure (rate of energy deposition 0.29 W/kg). By comparison with controls, efflux curves from field exposed brains were disrupted by waves of increased ⁴⁵Ca²⁺ efflux. These waves were irregular in amplitude and duration, but many exhibited periods of 20-30 min and continued into the post-exposure period. Binomial probability analysis indicates that the field-exposed efflux curves constitute a different population from controls at a confidence level of 0.96. In about 70% of cases, initiation of field exposure was followed by a transient increased end-tidal CO₂ excretion for about 5 min. However, hypercapnea induced by hypoventilation did not elicit increased ⁴⁵Ca²⁺ efflux. Thus this increase with exposure does not appear to arise as a secondary effect of raised cerebral CO₂ levels. Radioactivity measurements in cortical samples after superfusion showed ⁴⁵Ca²⁺ penetration at about 1.7 mm/hr, consistent with diffusion of the ion in free solution.

0345 LOW FREQUENCY AMPLITUDE MODULATED MICROWAVE FIELDS CHANGE CALCIUM EFFLUX RATES FROM SYNAPTOSOMES. (Eng.) Lin-Liu, S. (V.A. Hospital, 11201 Benton St., Loma Linda, CA 92357); Adey, W. R. *Bioelectromagnetics* 3(3):309-322; 1982 (24 refs).

Calcium (⁴⁵Ca²⁺) efflux from preloaded rat synaptosomes was studied with a continuous perfusion technique and the rate constants of a biphasic efflux process calculated. When synaptosomes were exposed to 16-Hz sinusoidally amplitude modulated 450-MHz microwave (MW) fields (maximal incident intensity 0.5 mW/cm², modulation depth 75%) during the second (slow) phase, the rate constant increased by 38%. Exposure to continuous wave or 60-Hz modulated fields did not produce similar results. The MW field-induced change can be distinguished from ⁴⁵Ca²⁺ efflux stimulated by calcium chloride injection which is most probably derived intracellularly. These data suggest that the MW field-induced change in calcium efflux probably did not involve intracellular calcium. Moreover, the sensitivity exhibited by synaptosomes, which can be regarded as subcellular neuronal elements, provides evidence that whole cells or organized tissue are not required as essential anatomical substrates for field-tissue interaction.

0346 FLUORESCENCE DEPOLARIZATION STUDIES OF THE PHASE TRANSITION IN MULTILAMELLAR PHOSPHOLIPID VESICLES EXPOSED TO 1.0-GHz MICROWAVE RADIATION. (Eng.) Allis, J. W. (MD-74, Experimental Biology Div., Health Effects Research Laboratory, EPA, Research Triangle Park, NC 27711); Sinha, B. L. *Bioelectromagnetics* 3(3):323-332; 1982 (16 refs).

To investigate the interaction of microwave (MW) radiation with lipid bilayer vesicles, multilamellar dimyristoylphosphatidylcholine (DMPC) vesicles were exposed to continuous wave 1.0 GHz MW energy in a temperature controlled rectangular TEM cell. Before exposure, a fluorescent lipid-seeking molecular probe, diphenylhexatriene (DPH), was introduced into the DMPC membranes. Since chloroform is known to shift phase transition to a lower temperature, DMPC vesicles were also treated with chloroform to serve as positive controls. Fluorescence depolarization measurements were made as a function of temperature on control samples and on DMPC suspensions exposed to 1.0 GHz at specific absorption rates (SAR) of 1, 5, 15, or 30 W/kg. Measurements were also performed over a series of power levels while the temperature was maintained at 23.5 and 25.5 °C; these temperatures represent the points at which shifts in the phase transition could be detected easily. Semilog plots of microviscosity versus temperature showed that phase transition temperature in chloroform-treated vesicles was 5 °C lower than in untreated controls. No shift of the phase transition was found during exposure to 1.0 GHz MW radiation at SARs between 1-30 W/kg. No statistically significant difference was found between exposed and control samples as SAR was increased. These results are in contrast to those of others using laser Raman spectroscopy to measure the phase transition in similar multilamellar vesicles exposed to MW radiation.

0347 POSTRESONANCE ELECTROMAGNETIC ABSORPTION BY MAN AND ANIMALS. (Eng.) Massoudi, H. (Dept. Electrical Engineering, Univ. Utah, Salt Lake City, UT 84112); Durney, C. H.; Barber, P. W.; Iskander, M. F. *Bioelectromagnetics* 3(3):333-339; 1982 (10 refs).

A surface integral equation (SIE) method is used to calculate the specific absorption rate (SAR) in spherically capped cylindrical models of man irradiated by an axially incident electromagnetic (EM) plane wave (K polarization) in the frequency range 80-400 MHz. In the SIE method, the EM field equations are formulated in terms of the electric and magnetic currents induced on the surface of the body and the resultant integral equation is solved by the method of moments. The forward scattering theorem is used to calculate the average SAR from the far scattered EM fields. SAR data calculated by the SIE method show good agreement with data calculated by the extended boundary condition method (EBCM) for frequencies up to 80 MHz (the upper frequency limit of the EBCM) for man models. For rat models exposed to 1-3 GHz radiation, reasonable agreement was also obtained with the limited experimental data available. The upper frequency limit for SIE is 400 MHz for man models and 3 GHz for rat models. When calculated average SAR values for the E and H polarizations were plotted with the data for the K polarization, it was found that the three curves intersect just above the E polarization resonance. This information may be useful in designing experiments where average SAR must be independent of animal position.

Current Literature

Biological Effects of Nonionizing Electromagnetic Radiation VII(2-4), July 1983

0348 EFFECTS OF 60-Hz ELECTRIC FIELDS ON SPECIFIC HUMORAL AND CELLULAR COMPONENTS OF THE IMMUNE SYSTEM. (Eng.) Morris, J. E. (Biology Dept., Pacific Northwest Laboratory, P.O. Box 999, Richland, WA 99352); Phillips, R. D. *Bioelectromagnetics* 3(3): 341-347; 1982 (20 refs).

The functional aspects of humoral and cell-mediated immunity in Swiss-Webster mice exposed to 60-Hz electric fields at 100 kV/m (20 hr/day for 30 to 150 days) were investigated. Mice were housed in plastic cages between parallel-plate electrodes (3 animals/cage). The mice were in electrical contact with the wire mesh floors of the cages which constituted the reference ground electrode. After 60 or 90 days, exposed, sham exposed, and cage control mice were immunized ip with keyhole limpet hemocyanin (KLH); assays for precipitating antibodies were taken 14 days after challenge. No significant differences were observed in primary antibody response to KLH among the three groups of mice after 30 or 60 days of exposure. Responses of spleen cells from exposed, sham-exposed, and cage control mice were compared for three mitogens (concanavalin A, pokeweed mitogen, lipopolysaccharide) at various concentrations after exposure periods of 90 and 150 days. No significant differences were observed among the three groups of mice in the 90-day and 150-day exposure. Mean stimulation indexes obtained for phytohemagglutinin-treated spleen cells appeared to be higher for the exposed group than for sham exposed controls; however, statistical evaluation of the data indicated that the difference was not statistically significant.

0349 POSSIBLE EFFECTS OF 1011 Hz RADIATION ON THE OXYGEN AFFINITY OF HEMOGLOBIN. (Eng.) Kondepudi, D. K. (Center for Studies in Statistical Mechanics, Dept. Physics, Univ. Texas, Austin, TX 78712). *Bioelectromagnetics* 3(3):349-361; 1982 (19 refs).

The possible effect of electromagnetic radiation on the hemoglobin molecule is examined and a simplified model for heme plane oscillations is developed. The binding of oxygen to one of the subunits of hemoglobin greatly enhances the oxygen affinity of the other subunits. This cooperative interaction of the subunits is initiated by the movement of the heme plane toward the proximal side when oxygen binds to the heme. This motion is transmitted to the surface of the globin through a "reaction path" consisting of a group of atoms whose motion is well correlated. A simple model for the heme plane oscillations is presented based on detailed geometry and x-ray diffraction data of the mean square displacement of the atoms surrounding the heme. Using this model, the natural frequency of oscillations is approximately 3 x 10¹¹ Hz. This result, along with recent experimental data on the kinetics of the conformational changes of the heme, points to the possibility that radiation may influence the oxygen affinity of hemo-

globin. If such an effect exists, it is likely that the oxygen affinity will be enhanced by the radiation.

0350 LOCAL TUMOR HYPERTHERMIA USING A COMPUTER-CONTROLLED MICROWAVE SYSTEM. (Eng.) Magin, R. L. (Dept. Electrical Engineering, Univ. Illinois, 1406 West Green Street, Urbana, IL 61801); Fu, T. S.; Beard, R. E.; Cain, C. A. *Bioelectromagnetics* 3(3): 363-370; 1982 (9 refs).

A minicomputer-based system designed to provide local heating to tumors in laboratory animals is described. The system was used to treat transplanted subcutaneous PARA-7 fibrosarcomas in female golden Syrian hamsters without occurrence of skin burns. A computer was programmed to control the average microwave (MW) power delivered to each of four local hyperthermia applicators in accordance with intratumor temperature measurements performed at the end of a specified interval of time when no MW power was applied. MW power (2.45 GHz) was delivered through dielectrically loaded MW applicators coupled to the tumors by a temperature-regulated water-coupling cuff. Temperature in each tumor was measured by thermocouples threaded through the center of the tumor. A temperature-scanning apparatus was used to determine the steady-state temperature distribution in tumors. After an initial rapid heating period of 2-3 min when MW power was 20 W, an average power of 4 W was required to maintain a steady state temperature of 43°C at the tumor center for 30 min; duty cycle was 0.78 and circulating water temperature in the water coupling cuff was 41°C. Use of the circulating water cuff reduced intratumor temperature gradients and eliminated skin burns.

0351 MEASUREMENT OF BLOOD-BRAIN BARRIER PERMEATION IN RATS DURING EXPOSURE TO 2450-MHz MICROWAVES. (Eng.) Ward, T. R. (EPA, MD-74, Experimental Biology Div., Research Triangle Park, NC 27711); Elder, J. A.; Long, M. D.; Svendsgaard, D. *Bioelectromagnetics* 3(3):371-383; 1982 (24 refs).

Adult CD albino rats were injected with a mixture of two radiolabeled saccharides (sucrose and inulin) and exposed for 30 min to 2450 MHz continuous wave microwave (MW) radiation in the far field of an anechoic exposure facility at 22°C at power densities of 0, 10, 20, or 30 mW/cm² or to an environment at temperatures of 22, 30, or 40°C. Following exposure, the brain was perfused and sectioned into eight regions, and the radioactivity in each region was counted. Data were analyzed both by a series of individual regression analyses to determine the response of each brain region to each tracer and by profile analysis to test for general changes. When the data were analyzed by 16 independent regression analyses and Bonferroni's method was applied to prevent false positive results from numerous analyses, no statistically significant

increase in permeation was found for either tracer in any brain region of MW-exposed rats. When a profile analysis was used to test for a general change in tracer uptake across all brain regions, a significant increase in permeation was found for sucrose but not for inulin. However, no significant increase in permeation due to MW exposure was found after a correction factor derived from the warm-air experiments was applied to the data for the MW-exposed rats. The results suggest that the increase in brain permeation to sucrose observed at higher SAR was due to the thermalizing effect of MW exposure.

0352 ELECTROMAGNETIC DOSIMETRY IN A SITTING RHE-SUS MODEL AT 225 MHz. (Eng.) Olsen, R. G. Naval Aerospace Medical Res. Lab., Code 41, Pensacola, FL 32508; Griner, T. A. *Bioelectromagnetics* 3(3):385-389; 1982 (7 refs).

A 9.5-kg tissue-equivalent rhesus model with an overall sitting height of 73.5 cm was exposed to continuous wave microwave (MW) power at 225 MHz in a horn and waveguide assembly placed inside an anechoic chamber. The model faced the horn at a distance of 228 cm. A nonperturbing temperature probe and a gradient-layer calorimeter were used to determine localized and whole body specific absorption rates (SAR). Normalized SARs based on temperature probe measurements showed deep penetration of MW energy, and calorimeter experiments showed an average SAR of 0.285 W/kg per mW/cm², a value much higher than the 0.107 W/kg per mW/cm² calculated for the same model at 1.29 GHz.

0353 THE VACUOLAR POTENTIAL OF CHARACEAN CELLS SUBJECT TO ELECTROMAGNETIC RADIATION IN THE RANGE OF 200-8200 MHz. (Eng.) Barsoum, Y. H. (c/o Pickard, Dept. Electrical Engineering, Washington Univ., St. Louis, MO 63130); Pickard, W. F. *Bioelectromagnetics* 3(4):393-400; 1982 (14 refs).

Single giant cells of *Chara braunii* and *Nitella flexilis* were placed in a microstrip exposure apparatus and subjected to bursts of electromagnetic radiation (carrier frequencies from 200 to 8,200 MHz) at a nominal power level of 100 W/m². The vacuolar potential was monitored with a micropipette, and offsets as low as 1 uV could be resolved in real time by suitable filtering and signal averaging. At the 100 W/m² power level, no visible resting potential offset was detected. However, when the power was increased to a nominal 200 kW/m² (i.e., 400 mW delivered to the microstrip or roughly 2.2 V rms on the line), the slow hyperpolarizing ramp reported at lower frequencies could be seen but could not be accurately measured because of insufficient power. It appeared to decay beyond 500 MHz and to be absent at and above 950 MHz. To investigate reports that snail neurons irradiated for 1 hr at 2450 MHz and approximately 15.5 W/kg de-

veloped lowered membrane resistivities, electrogenic and nonelectrogenic *Chara braunii* and nonelectrogenic *Nitella flexilis* cells were exposed in the microstrip apparatus for 1 hr at 2450 MHz and 230 W/m². Membrane resistivity decreased 19.3%, 18.9%, and 17.1%, respectively, for each cell type.

0354 SYSTEMS FOR EXPOSING MICE TO 2450-MHz ELECTROMAGNETIC FIELDS. (Eng.) Chou, C.-K. (RJ-30 Univ. Hosp., Seattle, WA 98195); Guy, A. W. *Bioelectromagnetics* 3(4):401-412; 1982 (13 refs).

Two systems for exposing mice to 2450-MHz microwave (MW) fields are described. Dosimetry data on the two systems are also presented. Laboratory animals are placed in individual holders made of a polypropylene beaker inserted into a low-loss Styrofoam cage for exposure. Since the systems are designed for short-term exposure, food and water are not provided. Animals are maintained in a constant temperature and humidity environment maintained by forced-air ventilation. A circular waveguide system is used to expose four mice simultaneously to circularly polarized electromagnetic fields. For 1-W input power to the waveguide, the average specific absorption rate (SAR) was determined by twin-well calorimetry to be 3.60 ± 0.11 W/kg in 27-g mice. The maximum SAR at the skin surface determined thermographically was 3.36 W/kg in the head of the mouse. A miniature anechoic chamber is used to expose six mice simultaneously to far-field plane waves. The inside of the chamber was lined with copper shielding and high-temperature absorbing material to accommodate high input power. The air ventilation at the location of the mice was separately controlled so that any heating in the absorber would not affect the animals. For 1-W input power, and when the animals were irradiated with body axis parallel to the E field, the average SAR was 0.17 ± 0.01 W/kg and the maximum SAR at the skin surface was 0.41 W/kg; when the animals were irradiated perpendicular to the E field, the SARs were 0.11 ± 0.01 W/kg and 0.64 W/kg, respectively. Although multiple scattering among the animals in the circular waveguide system is larger than in the anechoic chamber, the circular waveguide system offers some advantages over the anechoic chamber system: it is more energy efficient and less orientation dependent than the miniature chamber and it takes up less space.

0355 EVIDENCE FOR ELECTROSTATIC ENHANCEMENT OF ODOR RECEPTOR FUNCTION BY WORKER HONEYBEE ANTENNAE. (Eng.) Erickson, E. H. (Bee Management Investigations, US Dept. Agriculture, Science Education Admin., Russell Lab., Univ. Wisconsin, Madison, WI 53706). *Bioelectromagnetics* 3(4):413-420; 1982 (12 refs).

Pore plates (placoid chemosensillae) on the antennae

of dead worker honeybees (*Apis mellifera L.*) apparently retained a static electric charge that was significantly different from that of the surrounding cuticle. Residual charge resulted in the concentration of airborne particulate matter over the rim of exposed pore plates to the virtual exclusion of such deposition on surrounding cuticle. Postmortem integrity of polar lipids associated with the pore plate and adjacent sense cells is hypothesized as the source of the static potential. Such a lipidal matrix, if functioning as an electret and if attracting odorous molecules to receptor cells from outside the odor stream of individual receptors, would greatly enhance receptor efficiency of living bees.

0356 IN VIVO AND IN VITRO DIELECTRIC PROPERTIES OF ANIMAL TISSUES AT RADIO FREQUENCIES. (Eng.) Kraszewski, A. (c/o M.A. Stuchly, Non-Ionizing Radiation Sect., Environmental Health Centre, Health and Welfare Canada, Ottawa, K1A 0L2, Ontario, Canada); Stuchly, M. A.; Stuchly, S. S.; Smith, A. M. *Bioelectromagnetics* 3(4):421-432; 1982 (12 refs).

The dielectric properties of cat tissues *in vivo* and *in vitro* were measured and compared in the frequency range between 100 MHz and 8 GHz. The permittivity of rat tissues *in vivo* is also reported. An open-ended coaxial line and an improved measurement method employing a computer-controlled network analyzer were used. *In vivo* measurements were performed on four anesthetized cats; various tissues (muscle, spleen, kidney cortex, liver, and brain cortex) were surgically exposed for dielectric measurements. The cats were euthanized and submerged in a normal saline bath; individual tissues were raised just above the saline bath surface and blotted dry immediately before the measurement probe was applied to the same tissues. The differences between *in vivo* and *in vitro* (less than 4 hr after death) measurements of the dielectric constant and the conductivity of all cat tissues were found to be smaller than the experimental uncertainty limits of 2% for the dielectric constant and 3% for the conductivity. These results provide an experimental confirmation of the predicted behavior of tissues.

0357 FAR-FIELD DOSIMETRIC MEASUREMENTS IN A FULL-SIZED MAN MODEL AT 1.0-GHz. (Eng.) Olsen, R. G. (Naval Aerospace Medical Res. Lab., Code 41, Pensacola, FL 32508). *Bioelectromagnetics* 3(4):433-442; 1982 (11 refs).

Electromagnetic dosimetry was conducted in a tissue-equivalent full-sized (1.74 m, 70 kg) model of man irradiated at 2 GHz inside a microwave-anechoic chamber. A nonperturbing temperature probe and a gradient-layer calorimeter were used to determine local and whole-body specific absorption rate (SAR), res-

pectively. Temperature was measured in 9 locations in the body. Dosimetric data were taken at the front surface of each location and at 1 cm depths directly behind each location to give a profile of absorption. Relatively high SAR values were found in the limbs compared to the axis of the trunk of the model. Five whole body calorimetric determinations were made. The calorimeter experiments yielded an average SAR about 3-fold higher than that estimated theoretically for a prolate spheroidal model of man. It is suggested that resonant interactions involving the limbs may be responsible for the disparity between theory and experiment.

0358 A BEHAVIORAL RESPONSE OF SWINE TO A 60-Hz ELECTRIC FIELD. (Eng.) Hjeresen, D. L. (c/o Phillips, Biology Dept., Battelle Pacific Northwest Lab., Richland, WA 99352); Miller, M. C.; Kaune, W. T.; Phillips, R. D. *Bioelectromagnetics* 3(4):443-452; 1982 (13 refs).

Hanford miniature swine that had been exposed to a 60-Hz electric field at 30 kV/m for 20 hr/day, 7 days/wk for up to 3438 ± 45 hr, were tested for their preference for the presence or absence of the field during a 21-hr period. During behavioral testing, 4/17 exposed swine and 9/15 sham-exposed swine were pregnant. The swine were tested in a shuttlebox system consisting of a shielded and an unshielded stall connected by a passageway. The location of the pig within the shuttlebox was monitored with two light-beam scanners in the passageway. Each of the 32 pigs was subjected to a single 21 hr test, which included 2 light periods and a 12-hr dark period (from 5 PM to 5 AM). Known modes of indirect interaction between swine and 60-Hz fields were eliminated or reduced to very small values. Data were analyzed within the two light periods, the dark period, and the entire 21-hr period. Swine spent significantly more time in the region shielded from electric field exposure during the sleeping period of the diurnal cycle (5 PM-5 AM); when active, they moved between shielded and exposed regions fairly frequently and showed no significant preference for either side. The response of pregnant and nonpregnant pigs to electric field exposure appeared to be different: 11/13 exposed nonpregnant swine preferred the shielded side while the 4 pregnant swine exhibited no preferences. The behavioral response of swine in a 60-Hz electric field is similar to that in rats. It is suggested that the response is a result of a direct interaction between the electric field and the animals.

0359 EFFECTS OF X-BAND MICROWAVE EXPOSURE ON RABBIT ERYTHROCYTES. (Eng.) Cleary, S. F. (Dept. Biophys., Med. Coll. Virginia, Virginia Commonwealth Univ., Richmond, VA 23298); Garber, F.; Liu, L. M. *Bioelectromagnetics* 3(4):453-466; 1982 (11 refs).

The effects of continuous wave (CW) and pulsed microwave (MW) heating on the permeability of erythrocyte (RBC) plasma membranes were studied. RBC from adult Dutch rabbits were exposed as whole (heparinized) blood suspensions or as washed cells in 1:1 isotonic buffered K⁺-free saline suspensions in waveguide exposure chambers or in a temperature-controlled circulating water bath within 20 min after the blood samples were taken; duration of exposure was 2 hr. Temperature distributions within the samples were measured with either a Vitek electrothermia probe or a thermocouple. Statistically significant increases in K⁺ efflux compared to water-bath-heated controls were detected when RBC were exposed in whole blood suspensions to either CW or pulse-modulated 3.42-GHz MW energy at specific absorption rates (SAR) resulting in sample temperatures of 24.0 and 24.4°C, respectively. Pulsed MW exposure (5 usec pulses, equivalent peak power density of 14.5 W/cm² at the center of the waveguide, pulse repetition rates of 138, 413, or 555 Hz; SAR, 21.6 mW/g) resulted in a small but consistent enhancement of K⁺ efflux in 1:1 red cell suspensions and to a lesser extent in whole blood, compared with CW exposure (SAR, 21.7 mW/g). No statistically significant K⁺ efflux occurred in the case of 1:1 red cell suspensions under the same exposure conditions. Measured differences in sample heating rates and temperature gradients between MW-exposed and heated control suspensions may account in part for the differential effect of MW exposure, but such effects do not appear to fully explain the results of this study.

0360 ASSESSMENT OF THE IMMUNE RESPONSIVENESS OF MICE IRRADIATED WITH CONTINUOUS WAVE OR PULSE-MODULATED 425-MHz RADIO FREQUENCY RADIATION. (Eng.) Smialowicz, R. J. (Experimental Biology Div., Health Effects Research Lab., EPA, Research Triangle Park, NC 27711); Riddle, M. M.; Weil, C. M.; Brugnolotti, P. L.; Kinn, J. B. *Bioelectromagnetics* 3(4):467-470; 1982 (7 refs).

Groups of four female BALB/C mice (8-10 wk old) were irradiated with either continuous wave (CW) or pulse modulated (PM: 1-msec pulse width, 250 pulses/sec) 425-MHz radiofrequency (RF) radiation. Mice were irradiated for 1 hr on each of 5 consecutive days in a rectangular strip-transmission line at average forward powers of 78, 17.7, or 5 W for CW and 17.7, 5, or 1.25 W for PM. The mean specific absorption rate, as measured using twin-well calorimetry was 7.7 W/kg for a forward power of 70 W. No differences in the mitogen-stimulated response of lymphocytes or in the primary antibody response to sheep erythrocytes or polyvinylpyrrolidone were observed between irradiated and sham-irradiated mice, nor between mice exposed to either CW or PM 425-MHz RF radiation. The failure to detect a change in the immune response does not directly answer the question as to whether or not a qualitative difference in biological effectiveness exists between CW and PM modes.

0361 COMPARISON OF BACTERIAL GROWTH TO HIGH-INTENSITY MICROWAVE EXPOSURE AND CONVENTIONAL HEATING. (Eng.) Hossain, M. A. (c/o Dutta, Dept. Botany, Howard Univ., Washington, DC 20059); Dutta, S. K. *Bioelectromagnetics* 3(4):471-474; 1982 (4 refs).

Escherichia coli pol A⁺ and pol A⁻ strains were exposed in the far field to 8.8-GHz microwaves (MW) pulsed at 1000 Hz (1-usec pulse width) and an SAR of 40 W/kg, which increased the temperature of a 3-ml bacterial suspension by 7°C. Two-way analysis of variance showed no significant difference between the growth rates of MW-irradiated and thermally exposed cells beyond that associated with a temperature increase.

0362 ATTEMPTS TO ALTER $^{45}\text{Ca}^{2+}$ BINDING TO BRAIN TISSUE WITH PULSE-MODULATED MICROWAVE ENERGY. (Eng.) Merritt, J. H. (USAF/SAM, Brooks AFB, San Antonio, TX 78235); Shelton, W. W.; Charness, A. F. *Bioelectromagnetics* 3(4):475-478; 1982 (3 refs).

Experiments were designed to test the effect of both *in vitro* and *in vivo* exposure to pulse-modulated microwave (MW) energy on $^{45}\text{Ca}^{2+}$ binding in rat brain tissue. Six individual samples loaded with $^{45}\text{Ca}^{2+}$ by intraventricular injection were exposed to MW at 1 GHz (16 Hz pulse repetition rate, 20 msec pulse width, power densities of 1 or 10 mW/cm², specific absorption rates [SAR] of 0.29 or 2.9 W/kg), or 2.45 GHz (16-Hz pulse repetition rate, 20 msec pulse width, power density of 1 mW/cm², SAR = 0.3 W/kg), or sham radiation for 20 min. No significant differences between irradiated and sham-irradiated tissues with respect to $^{45}\text{Ca}^{2+}$ efflux were found. For whole animal exposures, rats were injected intraventricularly with $^{45}\text{Ca}^{2+}$ and exposed for 20 min to 2.06 GHz in one of 17 different combinations of power density and pulse repetition rate. Pulse width was held constant at 10 msec; SAR was 0.24 W/kg per mW/cm². There was no significant difference in efflux of $^{45}\text{Ca}^{2+}$ between MW- and sham-irradiated groups. The data indicate that net $^{45}\text{Ca}^{2+}$ efflux in rat brains exposed either *in vitro* or *in vivo* is not altered by pulse-modulated MW radiation under the conditions used in this study.

0363 MICROWAVE ABSORPTION BY FOLDED DNA CHAINS. (Eng.) Kohli, M. (Dept. Physics, Purdue Univ., West Lafayette, IN 47907); Van Zandt, L. L. *Biopolymers* 21(7):1399-1410; 1982 (8 refs).

The absorption of microwave radiation by a DNA molecule is calculated for a segment of a straight, semi-infinite polymer chain with abrupt, localized bends. The power absorbed by a segment of chain between two bends is calculated first. Every length of polymer

chain is then regarded as lying between bends and the calculated absorption can be integrated over the distribution of interbend distances. Contributions to cross section absorption from base pairs outside the bends are estimated separately. Vibrational properties of the bends were parameterized by a transmission and a reflection coefficient. A general Green's function expression for power absorption was studied for different damping rate values and for transmission and reflection coefficients. Detailed expressions for absorption cross sections for longitudinal and optical modes are presented in an appendix. The specific system for which absorption estimates were made is poly(dG)-poly(dC) in B-conformation. Curves of absorption vs frequency (5.0-30.0 GHz) are shown for various damping parameters and reflection conditions.

0364 ABSORPTION OF MICROWAVE RADIATION BY DNA DOUBLE HELIX IN AQUO. (Eng.) Van Zandt, L. L. (Dept. Physics, Purdue Univ., West Lafayette, IN 47907); Kohli, M.; Prohofsky, E. E. *Biopolymers* 21(7):1465-1468; 1982 (9 refs.).

The microwave absorption by DNA double helix in aqueous solution was calculated, and theoretical results were compared with experimental data. Elastic properties of the isolated, dry molecular chain were determined and organized into distinct normal modes characterized by wave number and by one of four eigenvectors in the microwave portion of the spectrum. The behavior of water was treated as a viscous, elastic, inertial continuum extending radially from the surface of a long cylindrical core to infinity. A general expression was obtained for fluid field velocity in the form of a series of independent vector fields. Calculated absorption values agreed strikingly with experimental values for the relative absorption of water and DNA solution at 8-12 GHz. In contrast to simple relaxation time models of molecule-solvent interaction, the theory predicts decreases in absorption at higher frequencies. Data for the narrow frequency range suggest that the drop may be even stronger than predicted, suggesting that additional mechanisms may be involved in the absorption process.

0365 A MICROWAVE RADIOMETRIC METHOD FOR THE STUDY OF THE SEMICONDUCTOR PROPERTIES OF LIVING TISSUE: ITS POTENTIAL APPLICATION TO TUMOR LOCATION. (Eng.) Bigu, J. (Elliot Lake Lab., Mining Res. Lab., PO Box 100, Elliot Lake, Ont., Canada). *Biotelem Patient Monit* 9(2):98-114; 1982 (26 refs.).

A microwave (MW) radiometric technique to enable investigation of the semi-conductive properties of biological tissue is described. The technique makes use of the nonlinear electric properties of tissue in conjunction with its radiative properties as described by

blackbody theory. Mixing of the MW power generated by a body region illuminated by MW energy with the MW power generated by an external source results in an intermodulation spectrum that can be measured with an intermediate frequency radiometer tuned to a predetermined difference frequency or a sum frequency of the intermodulation spectrum. Preliminary experimental results are presented. A radiometer operating at 225 MHz with a 10 MHz bandwidth was used in experiments conducted on rabbits, humans, MW absorbers, and dielectrics exposed to 9.3 GHz radiation at power density levels of 20 mW/cm² (less for human subjects). No increase in the 225-MHz signal took place from specimens illuminated in the 9.3-GHz field relative to the same specimens in the absence of the field. Results were limited by inadequate sensitivity of the radiometer; however, it was possible to establish an upper quantitative limit for effective semiconductor mixing parameters. Extension of the technique to tumor localization is discussed and described by a mathematical model. Radiometric scanning should detect differences in semiconductive properties at the boundary of the tumor and surrounding normal tissue.

0366 HYPERTHERMIA AS A TREATMENT FOR NEOPLASIA. (Eng.) Dreznik, A. (c/o Falk, 1-140 Gerrard Wing, Toronto General Hosp., Toronto, Ont. M5G 1L7 Canada); Falk, R. E.; Howard, V.; Makowka, L.; Venturi, D. *Can J Surg* 25(6):603-608; 1982 (88 refs.).

A review is presented of the historical background and experimental and clinical results of hyperthermia in cancer therapy. The reaction of tumor tissue to hyperthermia differs from that of normal tissue. Tumor cells are more sensitive to heat than normal cells at 42-44 C. Selective heating creates a core tumor temperature of 45-50 C with demonstrable tumor and vascular necrosis. The differences in heat accumulation in normal and malignant tissues are apparently related to tumor blood supply. Thermotherapy can be administered by whole body, regional, and local hyperthermia. Methods of production of hyperthermia for the treatment of malignant tumors include the use of the whole electromagnetic spectrum. Side effects of microwave and radiofrequency hyperthermia are summarized. Experimental studies suggest that hyperthermia produces an immunological response that plays a prominent role in tumor destruction. The mechanism of this effect is not known, but it may involve increases in cell membrane immunogenicity. A limited number of clinical trials of hyperthermia alone or in combination with chemotherapy or radiotherapy have been reported. Hyperthermia is synergistic with several chemotherapeutic agents, and there is evidence that it reduces the radiation dose necessary to cause tumor necrosis. Thermotherapy is effective with different histologic tumor types and with deep-seated as well as superficial tumors. Regional hyperthermia induced by radiofrequency offers the best and most controlled form of therapy.

0367 CLINICAL HYPERTHERMIA: RESULTS OF A PHASE I TRIAL EMPLOYING HYPERTHERMIA ALONE OR IN COMBINATION WITH EXTERNAL BEAM OR INTERSTITIAL RADIOTHERAPY. (Eng.) Manning, M. R. (Univ. Arizona Health Sciences Center, Radiation Oncology Div., Tucson, AZ 85724); Cetas, T. C.; Miller, R. C.; Oleson, J. R.; Connor, W. G.; Germer, E. W. *Cancer* 49(2):205-216; 1982 (35 refs).

Results of a Phase I trial of hyperthermia (HT) alone or in combination with high-dose-rate external beam or low-dose-rate interstitial radiotherapy in the treatment of 43 patients with advanced, locally accessible neoplasms refractory to conventional therapies are reported. HT alone was used in eleven patients who had reached radiation tolerance levels or were not candidates for radiation for other reasons. Seventeen patients with accessible lesions (who could tolerate general anesthesia) were treated with interstitial thermotherapy in which iridium or radium implants combined with HT produced by localized radiofrequency (RF) current fields using the implant guides or needle casings as electrodes. The remaining 15 patients were treated with externally produced HT and radiation. For all tumor types, HT alone (2-22 fractions, 42.5-44 C for 40 min) resulted in complete response (CR) in 2/11 patients (18%), partial response (PR) in 3/11 (27%); 6/11 patients showed less than 50% reduction in tumor volume. Of the nonresponders, 4/6 experienced growth arrest during treatment concomitant with pain relief. Duration of response was 1-24 mo. Of the patients treated with HT (43-44 C for 40 min at 72 hr intervals) followed by radiotherapy, 8/15 (53%) displayed PR, 4/15 (27%) showed CR, and 3/15 showed no response other than pain relief and central necrosis of tumor. Of the patients treated with interstitial thermotherapy, 5/17 (29%) showed PR lasting 2-3 mo and 12/17 (71%) displayed CR with no tumor regrowth within the treated volume for a 2-12 mo follow-up period. Total response rates based on tumor histology were 1/2 malignant fibrous histiocytoma, 3/5 sarcoma, 11/14 squamous cell carcinoma, 11/14 adenocarcinoma, and 8/8 melanoma. Complications were minimal for all treatment groups and included 1 third-degree burn and 3 second-degree burns from fringing RF fields, 1 vaginal-rectal fistula, a superficial focal soft tissue necrosis, and some minor blistering. The results demonstrate that HT alone or in combination with radiotherapy can be safely applied in the treatment of malignant disease. The data also suggest that HT, especially when combined with interstitial thermoradiotherapy, can yield remarkable results in the eradication of local cancers.

0368 THE TREATMENT OF CONGENITAL PSEUDARTHROSIS OF THE TIBIA WITH PULSING ELECTROMAGNETIC FIELDS: A SURVEY OF 52 CASES. (Eng.) Sutcliffe, M. L. (Orthopaedic Dept., Royal Hallamshire Hosp., Sheffield, S10, 2JF, England); Goldberg, A. A. J. *Clin Orthop* (166):45-57; 1982 (15 refs).

A survey is presented of European cases of congenital pseudarthrosis of the tibia treated with pulsing electromagnetic fields (PEMF) using the Bi-Osteogen System of Electro-Biology, Inc. Prior disability time of the 49 children (1-16 yr old, mean, 6.7 yr) was > 2 yr in 78% of the cases and > 5 yr in 35 % of the cases. All but 5 patients had undergone at least one unsuccessful surgical procedure (mean, 1.76 operations) before PEMF therapy was instituted. Of the 49 patients, a definite endpoint was reached in 37, and a successful outcome (union and progression to full wt bearing with protective orthosis) was achieved in 26 (70.2%). Of the 37 children who reached a definite endpoint, 28 patients with 30 fractures received an initial course of PEMF therapy alone; there were 15 successes (average treatment time, 7.7 mo) and 15 failures (average treatment time, 12.4 mo). Of the 15 failures, 7 responded to a bone graft and a second PEMF course (average treatment time, 8.6 and 8.86 mo, respectively, for the first and second treatment courses); 4 patients were awaiting surgery and further PEMF treatment. In 9 patients, initial PEMF therapy and surgery were carried out concomitantly; union occurred in 6 cases (average treatment time, 6.0 mo vs. 6.3 mo for 3 unsuccessful cases). Analysis of the results showed that PEMF therapy alone effected union in 60% of cases of Bassett Type I and 57% of Type II cases. An average treatment period of 6 mo is indicated before determining whether the coils will succeed in a given case. Although Type III cases with extreme atrophy and gross mobility do not respond to PEMF therapy alone, initial preoperative priming with PEMF is recommended. Because of the importance of effective immobilization and a strict, non-weight-bearing status, the applicability of PEMF therapy in young children (less than 33 mo old) is questionable.

0369 REWARMING MICE FROM HYPOTHERMIA BY EXPOSURE TO 2450-MHz MICROWAVE RADIATION. (Eng.) Gordon, C. J. (Physiology Section, Biological Engineering Branch, Experimental Biology Div., Health Effects Res. Lab., EPA, Res. Triangle Park, NC 27711). *Cryobiology* 19(4):428-434; 1982 (12 refs).

Effects of whole-body 2,450-MHz microwave (MW) heating on survival of hypothermic male AJ and CD-L albinos mice (25-40 g) were assessed. Body (colonic) temperatures were measured with a Vitek probe that provides unperturbed measurements in a radiofrequency radiation field (30-3000 MHz). The mice were cold-exposed in a cold waveguide system until body temperature decreased to an average of 25.7 C (range, 17-30 C). The MW generator was then activated and incident powers of 10-80 W were directed into the waveguide. Of 19 mice, 18 survived rewarming at rates of 0.04-0.65 C/sec. MW exposure caused tail burning (hot spots) in 12/19 animals, but the treatments apparently had no other ill effects. The one death that occurred was probably due to cold exposure (body temperature, 16.9 C). A warming rate of 0.65 C/sec is 17-200 times higher than rates achieved with external heating techniques such as immersion in warm water. Thus, inter-

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nal deposition of electromagnetic radiation permits far faster recovery of experimental animals from hypothermia.

0370 FOOD FORAGING OF HONEY BEES IN A MICROWAVE FIELD (2.45 GHz CW). (Eng.) Gary, N. E. (Dept. Entomology, Univ. California, Davis, CA 95616); Westerdahl, B. B. Environ Entomol 11(1):95-99; 1982 (15 refs).

The effect of exposure to 2.45 GHz continuous wave microwaves (MW) on the foraging behavior of honey bees was investigated. A population of cordovan honey bees was trained to fly 400 m from their colony to foraging arenas in an indoor laboratory containing identical treatment and sham MW chambers. The MW chamber simulated conditions anticipated within and surrounding proposed solar power satellite (SPS) rectennae. A 3-hr MW treatment was carried out on 5 consecutive days at 5 power densities (0, 5, 10, 20, and 40 mW/cm²). Bees made approximately 20-30 round trips during the 3-hr observation periods and were in the chambers for about half of the time. Mean daily foraging populations did not differ significantly for the MW and sham chambers. Mean round trip times and foraging time were similar for control and MW-treated bees at all power levels. MW-treated bees experienced no detectable alterations in orientation and navigation behavior. The results provide evidence that honey bees readily enter MW fields at power densities similar to and exceeding those expected to be present in the rectennae of the proposed SPS system (23 mW/cm² at the antenna center to 1 mW/cm² at the edge) and that their behavior is not adversely affected by these fields.

0371 COMMENTS ON THE PAPER "ENVIRONMENTAL POWER-FREQUENCY FIELDS AND SUICIDE." (2 LETTERS TO THE EDITOR). (Eng.) Smith, C. W. (Dept. Electrical Engineering, Univ. Salford, Salford M5 4WT, England); Baker, R. D. Health Phys 43(3):439-441; 1982 (3 refs).

According to Smith, recent work on the effects of low-frequency magnetic fields on bacteria growth rates suggests that there might be a critical onset magnetic field strength or a periodicity in propensity to suicide as a function of magnetic field strength (Perry et al; Health Phys 41:267-277; 1981). Statistical analysis of Perry's raw data confirmed the basic effect, but it neither confirmed nor ruled out the presence of periodicities. If there is any causal relationship between suicide and field strength, the size of the structural entity which should be sought for implication will be at least 360 μ M in diameter; local circuit neurons fall within this range. Baker's analysis of Perry's data confirms that the ratio of suicides to controls appears to oscillate with field

value indicating that the propensity to suicide at a given field value presumably either rises with the field, if the apparent oscillation is illusory, or does indeed oscillate. More study is needed.

0372 ABSORPTION CHARACTERISTICS OF PROLATE SPHEROIDAL MODELS EXPOSED TO THE NEAR FIELDS OF ELECTRICALLY SMALL APERTURES. (Eng.) Lekhtakia, A. (Dept. Electrical Engineering, Univ. Utah, Salt Lake City, UT 84112); Iskander, M. F.; Durney, C. H.; Massoudi, H. IEEE Trans Biomed Eng 29(8): 569-576; 1982 (20 refs).

Normalized average specific absorption rate (SAR) values were calculated for prolate spheroidal models of humans exposed to electrically small aperture sources. The incident electromagnetic fields in the aperture were replaced by those produced by equivalent electric and magnetic dipoles, depending on the character of the fields incident on the aperture. The induced fields within the spheroid produced by each dipole were determined using the extended boundary condition method (EBCM). The orientation of the induced electric field created by the dipoles at large distances from the aperture was parallel to the spheroid major axis. From the induced fields, the average SAR for the spheroid was calculated. All results were given in terms of aperture impedance, which is defined as the ratio of the incident normal electric field to the incident tangential magnetic field at the aperture. For all calculations, the aperture radius and incident power density were equal to .01 wavelength and 1 mW/cm², respectively. As the aperture location (the ratio of aperture-to-spheroid distance to wavelength) was increased at 27 MHz, the normalized average SAR decreased to approximately the same limiting value for different values of the aperture impedance. Calculations of the SAR were made at 10, 27 and 40 MHz and at an aperture location of 0.15, while the aperture impedance was varied in magnitude and phase. It is demonstrated that the nature of the near fields of the aperture source is more complex than that of elementary sources but that a qualitative understanding obtained from the study of the irradiation effects of an elementary source accounts for the near-field absorption characteristics of models irradiated by small aperture fields.

0373 AN ACCURATE PROBE FOR MAPPING STRONG HF MAGNETIC FIELDS. (Eng.) Oleson, J. R. (Div. Radiation Oncology, Arizona Health Services Center, Univ. Arizona, Tucson, AZ 85724). IEEE Trans Biomed Eng 29(8):581-583; 1982 (11 refs).

The design and use of a high frequency magnetic field probe with an accuracy of ± 5 percent and precision of ± 1 percent are described. The probe was designed for measuring magnetic fields over small areas and at

relatively high field strengths such as those used in hyperthermia treatment. The probe consists of a 1.5 cm diameter wire loop sensor constructed from the leads of a subminiature incandescent lamp. Light from the lamp is transmitted through a 2 m length of multi-fiber-optic cable. The probe measures the average orthogonal magnetic field components over a 2 cm² area. The probe does not allow for simultaneous measurements of orthogonal field amplitudes and relative phases. Since the probe is frequency dependent, its use without frequency spectrum analysis is only possible in fields of a well-defined single frequency such as the field produced by the Magnetrode (13.56 MHz). An expression was derived to relate the lamp intensity to magnetic field intensity, frequency and loop impedance and radius. For calibration purposes, the impedance of the wire loop was measured with the Hewlett-Packard 4315A Impedance Bridge. To test the calibration of the probe, calorimetry experiments were performed and field values were obtained from measurements with a Holiday Isotopic Field Probe at a frequency of 13.56 MHz using the Magnetrode body electrode. Both comparisons agreed to within the ± 5 percent accuracy of the probe.

7374 BLOOD FLOW EFFECTS ON THE TEMPERATURE DISTRIBUTIONS FROM AN INVASIVE MICROWAVE ANTENNA ARRAY USED IN CANCER THERAPY. (Eng.) Strohbehn, J. W. (Thayer Sch. Engineering, Dartmouth Coll., Hanover, NH 03755); Trembley, B. S.; Douple, E. B. IEEE Trans Biomed Eng 29(8):649-661; 1982 (39 refs).

The effects of variations in blood perfusion rates and tissue electrical properties on temperature distributions in homogeneous tissues produced by an array of invasive microwave antennas was studied by numerical simulations. The bioheat equation was solved numerically for a number of symmetrically-spaced antennas forming a circular array in a homogeneous two-dimensional tissue model. The electric field produced by each antenna was expressed as the field at the midpoint of a bare half-wave dipole embedded in a conductive medium. A constant heating of the tissue adjacent to the antenna of +5°C was assumed. The electrical properties of the modeled tissue were varied to simulate muscle, brain, and fat with the same antenna distribution. For a tissue model with the properties of muscle tissue, four antennas equally spaced about a 1.414 cm radius circle, a frequency of 1 GHz, and blood flow rates equal to or less than that in resting muscle tissue, steady state temperatures were reached within .5 min and temperature distributions were governed by heat conduction and were not significantly different from temperature distributions for no blood flow. For blood flow rates 10 times that in resting muscle tissue, steady state temperature distributions were reached within 5 min and the isotherm plots for the therapeutic temperatures were concentrated around the antenna. Temperature distributions were determined by blood flow and were significantly different from temperature distributions for

no blood flow. Temperature distributions for different frequencies are shown. For high blood flow rates, more antennas were needed to create an area of therapeutic temperature large enough to be effective in treating the tumor.

0375 MICROSTRIP LOOP RADIATORS FOR MEDICAL APPLICATIONS. (Eng.) Bahl, I. J. (International Telephone and Telegraph, Electro-Optical Products Div., 7635 Plantation Rd., Roanoke, VA 24019); Stuchly, S. S.; Lagendijk, J. J. W.; Stuchly, M. A. IEEE Trans Microwave Theory Tech 30(7):1090-1093; 1982 (9 refs).

Three microstrip loop radiators designed for medical applications are described. Two of them were designed for inducing local hyperthermia at 433 and 915 MHz, and the third was constructed for the detection of breast cancer using microwave radiometry at 1300 MHz. The design principles of the loop radiators and their dimensions under various loading conditions are presented together with a diagrammatic representation of their geometry. Return loss measurements with a network analyzer indicated that the radiators were well matched in a relatively broad range of frequencies, when placed in contact with the human female breast, a muscle phantom, and a distilled water bolus followed by a muscle phantom. Heating patterns of the 433 and 915 MHz radiators investigated by thermography as well as by liquid crystal films indicated that the heating patterns of these radiators placed in direct contact with the muscle phantom were assymetrical with respect to the axis of the radiator. This was attributed to the near-field effect created by the higher order modes. Temperature distribution in the phantom along the main axis, after irradiation by a 100-W, 30 usec pulse at frequencies of 433 and 915 MHz showed an exponential decrease with the distance from the surface. With the water bolus, the heating pattern of the radiators was symmetrical with respect to the axis. The penetration depth of the heating depended on the frequency of operation and the size of the radiator: it was 1.6 cm for the 433-MHz radiator and 1.1 cm for the 915-MHz radiator.

0376 CLINICAL RF HYPERTERMIA BY MAGNETIC-LOOP INDUCTION: A NEW APPROACH TO HUMAN CANCER THERAPY. (Eng.) Storm, F. K. (Div. Oncology, Dept. Surgery, UCLA Sch. Medicine, Univ. California, Los Angeles, CA 90024); Elliott, R. S.; Harrison, W. H.; Morton, D. L. IEEE Trans Microwave Theory Tech 30(8):1149-1152; 1982 (43 refs).

Classical methods for raising tissue temperatures are reviewed and the development and clinical use of Magnetrode magnetic-loop induction hyperthermia for cancer therapy are described. The magnetrode was designed so that the E-lines run parallel to tissue in-

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terfaces and overheating of fat and skin layers is minimized. The magnetrode is constructed from a conducting sheet rolled so that the two ends overlap but do not touch. The overlap area and distance between the ends determine the capacitance of the applicator. For homogeneous tissue phantoms placed within the magnetrode, peripheral heating of the phantom is much greater than the central heating. When high-dose hyperthermia was quickly applied to anesthetized dogs, temperature distributions within the abdominal cavity were similar to those in homogeneous phantom models. Moderate dose hyperthermia heated the central and peripheral tissues more evenly with a temperature gradient of less than 1°C. The effect of blood flow was demonstrated by applying moderate dose hyperthermia to the same dog when alive and dead which resulted in even heating and preferential peripheral heating, respectively. Deep heating with little surface heating was produced in a human thigh placed within the magnetrode. Of 89 tumors treated in clinical trials, 78% were heated to temperatures equal to or greater than 42°C, 36% to temperatures over 45°C and 25% to temperatures over 50°C without raising normal tissue temperatures beyond physiological limits. Success rates for reaching therapeutic temperatures are also given according to malignancy type and tumor size. Larger tumors had greater success rates which may reflect a decrease in their vascularization and thermoregulation. The clinical trials indicated that increasing the treatment time, temperature, and number of treatments increased the chance of tumor necrosis. Magnetic-loop induction hyperthermia producing 500-1000 W of absorbed power resulted in physiological changes which did not exceed physiologically tolerable limits. Surface tissue injury occurred in 0.3% of the treatments.

0377 HEAT TRANSFER IN SURFACE-COOLED OBJECTS SUBJECT TO MICROWAVE HEATING. (Eng.) Foster, K. R. (Dept. Bioengineering, Univ. Pennsylvania, Philadelphia, PA 19104); Ayyaswamy, P.; Sundararajan, T.; Ramakrishna, K. IEEE Trans Microwave Theory Tech 30(8):1158-1166; 1982 (15 refs).

A model to predict the thermal characteristics of a biological sample uniformly heated by an electromagnetic (EM) field and cooled by an unbounded, laminar fluid flow around the sample is described. The homogeneous biological sample was initially at a temperature equal to that of the coolant before EM heating began. The coolant was assumed not to be heated by the EM field. Objects of three geometries (sphere, cylinder, and rectangular slab) were analyzed. For each case, the solution of the appropriate non-dimensional differential equation for heat conduction with convective boundary conditions was presented. Actual temperature can be found assuming that the sample density, material thermal properties of the sample and the Biot and Reynolds numbers that characterize the flow and convective cooling, are known. Plots of non-dimensional temperature as a function of nondimensional time are shown for different locations within the

three differently shaped objects and for different Reynolds numbers of flow. An optimum flow rate beyond which no more effective cooling of the sample is possible exists for each situation and depends on the thermal conductivity of the object and coolant, and Prandtl number. Bounds were formulated for the maximum temperature difference produced within a sample that are possible for various flow situations as a function of sample size and thermal conductivity. The results are of general applicability and are also valid where the coolant is a gas or liquid different from water with the only restriction being the Reynolds number of flow.

0378 HUMAN WHOLE-BODY RADIOFREQUENCY ABSORPTION STUDIES USING A TEM-CELL EXPOSURE SYSTEM. (Eng.) Hill, D.A. (Radiation Biology Section, Defence Res. Establishment Ottawa, Ottawa, Canada K1A 0Z4). IEEE Trans Microwave Theory Tech 30(11):1847-1854; 1982 (31 refs).

A transverse electromagnetic (TEM)-cell exposure system constructed for the measurement of whole-body absorption in humans of radiofrequency radiation at frequencies of 3 to 20 MHz is described. Human volunteers were exposed to 11 $\mu\text{W}/\text{cm}^2$ for up to 1 hr/day, and never absorbed more than 1 W. The exposure chamber was a large (6.1 x 7.3 x 13.0 m) low-loss rectangular-coaxial TEM mode transmission line sharply tapered at each end to form a cell. The cell allows irradiation of subjects in any orientation with respect to the propagating TEM mode under simulated free space or grounded conditions. The absorbed power, determined from 3-min signal-averaged measurements of incident, reflected, and transmitted power, was measured to a precision of 0.06% of incident power (0.03 dB in insertion loss). Analysis of systematic errors in the method showed that a directional-coupler directivity approaching 50 dB is necessary for high accuracy in absorbed-power measurements and that any dielectric-loading effect of the subject on the cell absorption is undetectable. The total systematic error in determining absorption rate per unit exposure rate was about $\pm 35\%$ of the measurement. Operating frequencies are currently limited to 3-20 MHz due to occurrence of the first cell resonance, associated with the TE₀₁ mode, at 20.7 MHz. The first set of human whole-body absorption results is presented for 3 subjects exposed in free space to 11 $\mu\text{W}/\text{cm}^2$ at 18.5 MHz in six different body orientations with respect to the TEM wave. The measured absorption rates for the two principal E orientations are larger than the published predictions by a factor of 2-3.

0379 A BROAD-BAND TEMPERATURE-CONTROLLED SYSTEM FOR THE STUDY OF CELLULAR BIOEFFECTS OF MICROWAVES. (Eng.) Riazi, A. (Dept. Electrical Engineering, Univ. Utah, Salt Lake City, UT 84112); Hill, W.; Hagmann, M.J.; Gandhi, O.P.; J'Andrea, J.A. IEEE

Trans Microwave Theory Tech 30(11):1996-1998; 1982 (5 refs).

A broad-band temperature-controlled microwave (MW) exposure system designed for the study of cellular bioeffects of MW radiation is described. The dual-circuit apparatus allows simultaneous testing at frequencies in the E-band (65-75 GHz) and in the U-band (38-48 GHz). A waveguide switch is used in both circuits to allow accurate measurement of incident power levels with thermistor detectors. Continuous monitoring of both incident and reflected power is done with SWR meters connected to the broad-band diodes attached to directional couplers in the two circuits. A schematic of the irradiation system is presented together with diagrams of the system's thermally insulated housing and sample holders. The system coupling efficiency is greater than 99% over all useable frequencies, which allows use of relatively inexpensive low-power sources, and it is simple to operate. Opposing thermocouples allow measurement of temperature differences as small as ± 0.01 C. Compensatory heating of the control sample holders suggests that temperature differences over the course of 30 min exposures can be kept within ± 0.02 C by appropriate feedback circuits. The system has been successfully used to investigate the effects of MW radiation on cell suspensions of several bacterial strains. A limitation of the apparatus is that it exposes biological samples during their time of transit past the waveguide.

0380 MICROWAVE DIFFRACTION TOMOGRAPHY FOR BIOMEDICAL APPLICATIONS. (Eng.) Bolomey, J. C. (Laboratoire des Signaux & Systemes, Ecole Superior d'Electricite, Plateau du Moulon, 91190 Gif-Sur-Yvette, France); Izadnegahdar, A.; Jofre, L.; Pitchot, C.; Petronnet, G.; Solaimani, M. IEEE Trans Microwave Theory Tech 30(11):1998-2000; 1982 (11 refs).

A method for rapid microwave tomography for biomedical imaging applications is described. Electromagnetic energy scattered from the target was measured using a modulated scattering technique, which employed an array of probes that were loaded by nonlinear elements. Modulating the load resulted in a diffracted signal that was proportional to the field being measured and was collected by an auxiliary antenna. The image was calculated as the convolution product of the pointspread function of the focusing system and the equivalent current distribution function induced by the target which in turn was related to the scattered field intensity distribution. The experimental equipment consisted of a 10 mW generator with standard S-band waveguide, a linear probe array of 64 dipoles loaded by diodes and separated from each other by $\lambda/5$ at 3 GHz, a network analyzer, a minicomputer and a low-noise amplifier. Results were given for a target consisting of two plexiglass rods surrounded by water, a plexiglass rod surrounded by sponge and a

plexiglass cylinder filled with water. This method allowed measurements of the field on a measurement line within one-half sec and calculation of the image in 50 sec. Incident power levels were less than 1 mW/cm² and a spatial resolution of $\lambda/2$ was possible, where λ is the wavelength of the microwave energy in water (1.16 cm at 3 GHz).

0381 NUMERICAL AND EXPERIMENTAL RESULTS FOR NEAR-FIELD ELECTROMAGNETIC ABSORPTION IN MAN. (Eng.) Chatterjee, I. (Dept. Electrical Engineering, Univ. Utah, Salt Lake City, UT 84112); Gandhi, O. P.; Hagmann, M. J.; IEEE Trans Microwave Theory Tech 30(11):2000-2005; 1982.

An empirical formula for the mass-normalized whole-body-average electromagnetic energy (SAR) was derived for a 180-cell block model of man exposed to near fields with N-polarization (E-field directed arm to arm). A similar formula for P-polarization (no component of the E-field directed arm to arm) had already been derived. The SAR predicted from the empirical formulas agreed well with experimental results obtained by exposing reduced-scale models of humans to leakage fields similar to those from an RF sealer. Saline-filled figures were exposed to fringing fields from two metal parallel plates separated by Styrofoam and connected to a RF power generator producing 40-80 W of power at simulated frequencies of 71-176 MHz. The SAR was determined from the average temperature rise in the figure. In another set of experiments, a tissue phantom made of water, polyethylene powder, Superstuff (a gelling agent) and salt was placed in the figure. The internal E-fields in the figures measured with an implantable probe at three simulated frequencies (77, 110 and 150 MHz) were an order of magnitude less than the incident E-field and agreed well with the calculated E-fields. For 180-cell block models of man exposed to a 1 V/m RMS and 27.12 MHz vertical electric field, the model in contact with the ground plane had an SAR that was 8.5 times larger than the SAR for a model isolated by 5 cm from the ground plane.

0382 MICROWAVE POWER ABSORPTION IN A BIOLOGICAL SPECIMEN INSIDE A STANDING-WAVE IRRADIATION WAVEGUIDE. (Eng.) Fujiwara, O. (Dept. Electrical Engineering, Faculty of Engineering, Nagoya Univ., Furo-cho, Chikusa-ku, Nagoya 464, Japan); Amemiya, Y. IEEE Trans Microwave Theory Tech 30(11):2008-2012; 1982 (15 refs).

Expressions for the total absorbed power and the spatial distribution of absorbed power were derived for a prolate spheroidal model of a biological sample irradiated by standing waves in a rectangular waveguide. Three orientations of the spheroid were examined: the major axis of the spheroid parallel to the

electric field, parallel to the magnetic field and perpendicular to the electric and magnetic fields. The power absorption due to electric and magnetic fields were analyzed separately. Calculations from the theoretical expressions were made for a spheroidal model of a pupa with a major axis and radius of 15 and 5 mm, respectively, and a relative permittivity of 30-13; at a frequency of 2450 MHz. For all orientations of the spheroid, the power absorption produced by the electric field was larger than that produced by the magnetic field. The largest occurred when the electric field was parallel to the major axis of the spheroid. For all cases, the absorbed power was much less than the forward waveguide power. Exposure to electric fields did not create any spatial variation in power absorption, but exposure to magnetic fields did. The theoretical results for total absorbed power were compared with experimental results from pupa of *Tenebrio molitor* irradiated in a WRJ-2 waveguide (forward power, 10 W; frequency, 2485 MHz). The temperature increase of the pupa was measured with a chromel-alumel thermocouple to find the total absorbed power. The calculated values for total power absorption agreed well with the experimental values.

0383 EFFECT OF CHRONIC MICROWAVE RADIATION ON RABBIT ERYTHROCYTES. (Eng.) Nageswari, K. S. (Dept. Physiology, GSVM Medical Coll., Kanpur 208 002, India); Tandon, H. C.; Varma, S.; Bhatnagar, V. M. Indian J Exp Biol 20:13-15; 1982 (11 refs).

The effects of chronic microwave (MW) exposure (2.1 GHz, continuous wave, 5 mW/cm², for 3 hr/day, 6 day/wk for 3 mo) on peripheral blood were investigated in 13 rabbits. Blood samples from 8 irradiated and 5 control animals were collected preirradiation, at 1 and 2 mo, at the termination of the irradiation period, and 1/wk for 2 wk. The mean rectal temperature which was measured before and after each MW exposure during the entire 3 mo period did not increase more than an average 0.8 °C after each session of MW irradiation. Erythrocyte counts declined 4.27%, 8.08%, and 8.46% following 1, 2, and 3 mo exposure, respectively. Although recovery was seen in the 2 wk post-irradiation period, the cell count did not return to its initial value. Decreases in erythrocyte number were paralleled by increases in mean corpuscular volume and hemoglobin which became statistically significant at the end of 2 and 3 mo of MW exposure. These findings suggest that the animals may have been protected from hypoxia by the increases in size and hemoglobin content of the red cells.

0384 EFFECT OF PROLONGED LOW POWER MICROWAVE RADIATION ON PERIPHERAL LEUCOCYTE COUNTS IN RABBITS. (Eng.) Nageswari, K. S. (Dept. Physiology, GSVM Medical Coll., Kanpur 208 002, India); Tandon, H. C.; Varma, S.; Bhatnagar, V. M. Indian J Med Res 75: 453-459; 1982 (15 refs).

The effects of chronic exposure to low power density continuous wave microwave (MW) radiation (2.1 GHz, 5 mW/cm², 3 hr/day, 6 days/wk for 3 mo) on rabbit peripheral leukocytes were studied. Blood samples from 8 irradiated and 5 control animals were collected preirradiation (PRI), at 1 and 2 mo, at the termination of the irradiation period, and 1 wk for 2 wk. The mean rectal temperature was measured before and after each MW exposure during the entire 3 mo period and did not increase more than an average 0.8 °C after each time. After 3 mo exposure, total leukocyte counts increased 50% from PRI values of 6621 to 9825, and differential leukocyte counts revealed a threefold increase (from 5.75 to 14.13) in large lymphocytes and a significant decrease (from 53.5 to 45.25) in small lymphocytes. However, the counts returned to normal within 2 wk of termination of exposure. MW irradiation for 2 mo produced significant neutropenia which was corrected after exposures were continued for another mo. A significant but reversible leucocytosis was observed in rabbits after chronic exposure to low level MW radiation. In the absence of a thermal effect, the possibility of a specific cumulative effect at MW at low levels is considered.

0385 LOCALIZED HYPERHERMIA IN THE TREATMENT OF CANCER. (Eng.) Storm, F. K. (Div. Oncology, Dept. Surgery, UCLA Sch. Medicine, Univ. California, Los Angeles, CA 90024); Morton, D. L. Int Adv Surg Oncol 5:261-275; 1982 (58 refs).

Experimental and clinical studies of localized hyperthermia in cancer therapy are reviewed. Localized hyperthermia techniques include hot water bath, isolated limb perfusion, low frequency current fields, ferromagnetic coupling, ultrasound, microwaves (433, 915, and 2,450 MHz), and radiofrequency waves (13.56-27.1 MHz) using capacitive electrodes, induction coil, and magnetrode magnetic loop applicators. Recent clinical trials suggest that potentially effective hyperthermia can be achieved in most superficial and visceral solid human tumors regardless of histopathologic type, although it is most effective for large tumors. Local toxicity depends on the heat dose and the method of hyperthermia. Future hyperthermia potential as adjuvant therapy in surgery, and in combination with radiotherapy and with chemotherapy is summarized.

0386 DEMONSTRATION OF A THERMAL EFFECT OF MICROWAVES DURING LOW-LEVEL RADIATION. (Eng.) Klein, M. S. (Div. de Neurophysiologie Appliquée, Centre d'Etudes et de Recherches de Médecine Aérospatiale, 26 boulevard Victor, 75996 Paris Armées, France); Steru, L.; Milhaud, C. L. IRCS Med Sci 10 (6):455-456; 1982 (10 refs).

Effects of low-level microwaves (MW) on hypothermia induced by oxotremorine (OX: 125 mg/kg) or by apomor-

phine (AP: 16mg/kg) and on the blood-brain barrier (BBB) were studied in male C57BL mice. In one experiment, the anti-cholinergic agent methylatropine (which normally does not pass through the BBB) was injected simultaneously with OX. The mice were irradiated for 30 min at 2,450 GHz (continuous wave; 2 and 5 mW/cm²). MW exposure resulted in significant heating of mice made hypothermic by OX or AP; rectal temperatures in irradiated mice were significantly higher than those of control mice. MW did not antagonize OX-induced hyperthermia and, therefore, could not have crossed the BBB. These results are inconsistent with the existence of nonthermal MW effects at power densities lower than 10 mW/cm².

0387 AUDITORY PERCEPTION OF RADIO-FREQUENCY ELECTROMAGNETIC FIELDS. (Eng.) Chou, C.-K. (Bioelectromagnetics Res. Lab., Dept. Rehabilitation Medicine, Sch. Medicine, Univ. Washington, Seattle, WA 98195); Guy, A. W.; Galambos, R. J Acoust Soc Am 71(6):1321-1334; 1982 (55 refs).

Research on radiofrequency hearing, including psychological studies of human subjects, physiological and behavioral observations on animals, and physical measurements on materials is summarized. Humans with normal high-frequency hearing experience an auditory sensation when exposed to pulsed microwaves (MW) of sufficient energy content. A clicking, buzzing, or hissing sound is heard, depending on modulation characteristics of the MW. The perceived sound (for pulses less than 50 usec) seems to originate at the central, posterior aspect of the head. The threshold energy density per pulse is very low (2-40 μ J/cm²) and the maximal rise in temperature of the exposed tissue is 10^{-5} - 10^{-6} C for exposure of an individual pulse at the threshold energy density. Experimental data on cochlear potentials, single-unit nerve fiber responses, and brainstem evoked responses suggest that pulsed MW radiation produces cochlear microphonic responses similar to those elicited by other stimuli. Results of single unit recording of extra-cellular potentials in cats are consistent with human perceptions when pulse widths are long. Electrophysiological recordings from mammals have confirmed the mechanical nature of the MW hearing effect and are consistent with a mechanism of hearing based on thermoelastic expansion. Behavioral studies indicate that rats can perceive pulsed MW energy; results may be attributed to the hearing effect. However, the low threshold of the MW hearing phenomenon makes it essential to differentiate the hearing effect from other biological effects of pulsed MW radiation.

0388 POSTNATAL FUNCTIONAL ANALYSIS OF PRENATAL EXPOSURE OF RATS TO 915-MHz MICROWAVE RADIATION. (Eng.) Jersh, R. P. (Dept. Anatomy, Jefferson Medical Coll., Thomas Jefferson Univ., 1020 Locust St., Philadelphia, PA 19107); Vogel, W. H.;

Brent, R. L. J Am Coll Toxicol 1(3):73-90; 1982 (31 refs).

The effects of chronic prenatal continuous wave microwave (MW) exposure (915 MHz, 10 mW/cm², for 6 hr/day, days 1-21 of gestation) on postnatal neurological and neurobehavioral development were studied in Wistar albino rats. Animals delivered and raised their offspring (F_{1a}) until weaning at 30 days of age. Ten days after weaning, the mothers were rebred and allowed to deliver again (F_{1b} offspring). Irradiated neonates (F_{1a}) were given four perinatal reflex tests (surface righting, air righting, auditory startle, visual placing) and a physiological test (eye opening). At 60 days of age, F_{1a} offspring were given behavioral tests and at 90 days half of them were bred to determine reproductive capability and half were killed for histopathological studies. Prenatal irradiation significantly accelerated onset of reflex achievement. However, eye opening did not differ in experimental and control groups, suggesting that the acceleration may not have been simply a whole-body acceleration. Auditory startle was accelerated by 4.2 days. There were no significant differences between irradiated and control animals in 5/6 behavioral tests (water T-maze, open field, activity wheel, forelimb hanging, swimming); results of conditioned avoidance response tests revealed a decrease in long-term memory in exposed animals, but the variation in individual animals was quite high. Irradiation did not significantly affect maternal organ wt or organ-body wt ratios, and it did not alter neonatal and young adult growth rates. The results indicate that chronic prenatal exposure to low power density levels of 915 MW radiation did not result in any significant alterations of postnatal behavior or of growth and development.

0389 TREATMENT OF THERAPEUTICALLY RESISTANT NON-UNIONS WITH BONE GRAFTS AND PULSING ELECTROMAGNETIC FIELDS. (Eng.) Bassett, C. A. L. (Dept. Orthopaedic Surgery, Columbia Univ. Coll. Physicians & Surgeons, 630 West 168th St., New York, NY 10032); Mitchell, S. N.; Schink, M. M. J Bone Joint Surg [Am] 64(8):1214-1220; 1982 (18 refs).

The results of the combined and concomitant use of bone grafts and pulsing electromagnetic (EM) fields as a means of achieving bone union in 83 adults are reported. The patients consisted of 38 individuals with wide gaps, synovial pseudarthrosis and malalignment who had not undergone previous EM treatment (median disability time, 16 mo; 100 unsuccessful earlier surgical attempts at repair prior to treatment) and 45 individuals who had initially been unsuccessfully treated with pulsing EM fields alone (median disability time, 17 mo; 101 previous operations, including 38 bone grafting procedures). The majority of the lesions in both groups were tibial (45/83) and femoral (25/83) non-unions. Home treatments (10 hr/day) using a pulse generator that produced a 5 msec wide

burst of 200 usec wide (positive-going) pulses, repeating at 15 Hz began 2-4 wk postoperatively. Successful bone healing was seen in 33/38 (87%) patients without prior EM treatment and in 42/45 (93%) patients exposed to EM fields before and after grafting. The median time from start of EM-field treatment to healing was 4 mo in both groups. No complications of surgery or of pulsing EM fields were reported. Pulsing EM fields should receive strong consideration as an adjunct to any bone graft of the extremities, whether in a primary or a salvage situation.

0390 THE TREATMENT OF FIBROUS NON-UNION OF FRACTURES BY PULSING ELECTROMAGNETIC STIMULATION. (Eng.) Sharrard, W. J. W. (Royal Hallamshire Hosp., Glossop Rd., Sheffield S10 2JF, England); Sutcliffe, M. L.; Robson, M. J.; MacEachern, A. G. *J Bone Joint Surg [Br]* 64(2):189-193; 1982 (15 refs).

Results of pulsed electromagnetic (EM) stimulation in the treatment of 53 fibrous non-unions in 52 patients (25 male, 17 female, 13-79 yr old, mean age 37 yr) are reported. Median time from injury to start of treatment was 28.2 mo (range 1-25 yr). The tibia was the most commonly affected bone. An electric current of highly specific shape, magnitude and repetition rate was generated in the bone by a pair of externally-placed oval air-cored electromagnets driven by a small portable generator producing a 5-msec burst of quasi-rectangular assymetrical pulses repeated at 15 Hz. Patients were instructed to use the equipment for 12 to 16 hr/day. Union was achieved in 38/53 cases (71.7%) including 26/30 (86.7%) tibia fractures. The median time taken to reach union was 6 mo (range 3-16 mo). The results were not affected by patient age, previous or active sepsis, presence of plates or nails, or the time since injury. Inadequate immobilization, a gap between bone ends in excess of 5 mm, or a screw in or very near the fracture non-union site were the most important factors in the 15 failures. The results indicate that EM stimulation applied in conjunction with adequate immobilization promotes bone union in a high proportion of extremely refractory cases of ununited fractures or surgical insults.

0391 CYTOGENETIC CONSEQUENCES OF MICROWAVE IRRADIATION ON MAMMALIAN CELLS INCUBATED IN VITRO. (Eng.) Yao, K. T. S. (Bureau Radiological Health, FDA, Rockville, MD 20857). *J Hered* 73(2): 133-138; 1982 (33 refs).

A 2450-MHz microwave (MW) oven was converted into an incubator that also served as a MW exposure chamber. The effects of continuous MW exposure on growth and on chromosome structure of rat kangaroo RH16 cells (normal euploid chromosome number) and RH5 cells (hypoploid) were investigated. The cells were grown in the incubator at 35-37°C and simultaneously exposed

to MW irradiation for 320 days (50 passages) at an energy absorption dose rate of 15.2 ± 1.82 mW/g. Cells were then returned to a conventional incubator and allowed to grow for another 30 passages. MW-incubated and control cells were examined for chromosome aberrations at about 10, 20, 30, 40, and 50 passages of subculture. MW incubation resulted in a significant reduction of cell growth rates and an increase in cell doubling time. These effects appeared to be cumulative, with 15-passage irradiated cells exhibiting greater growth retardation and longer cell doubling time than 7-passage cells. Chromosome aberrations appeared after 20 passages (124 days) under irradiation. The number of chromosome breaks/cell reached a maximum of 0.84 in RH5 cells and 0.10 in RH16 cells. The former was hypoploid at the beginning of the experiment, which may have contributed to the greater susceptibility of this cell line to MW exposure. After the cell cultures were returned to the conventional incubator and maintained for 30 passages, the number of chromosome breaks was greatly reduced. MW irradiation altered the chromosome number of the cells. After the irradiation, RH5 and RH16 cell cultures had 35% and 31% polyploid cells, respectively. After long-term irradiation, 41% of RH5 cells which originally had 11 chromosomes became 10-chromosome cells. When the irradiated cells were returned to the conventional incubator, the percent of 10-chromosome cells reached 59%. The missing chromosome was usually chromosome 4.

0392 EVIDENCE FOR GENETIC CONTROL OF MICROWAVE-INDUCED AUGMENTATION OF COMPLEMENT RECEPTOR-BEARING B LYMPHOCYTES. (Eng.) Schlagel, G. J. (Armed Forces Inst. Pathology, Washington, DC 20306); Ahmed, A. *J Immunol* 129(4):1530-1533; 1982 (14 refs).

The genetic control of microwave (MW)-induced increase in complement receptor-bearing B lymphocytes (CRL) was studied in congenic, backcross, and recombinant inbred (RI) strains of mice. Mice were exposed to 2450 MHz MW radiation (0.6 W; 10-14 W/kg) in an environmentally controlled waveguide and assayed for CRL on days 3 or 6 postexposure. Genetic studies of responder X non-responder F₁ mice and backcross analysis of nonresponder X (responder x nonresponder)F₁ mice indicated that MW susceptibility was controlled by a single, dominant Mendelian gene. Crosses between two nonresponder strains failed to restore the responder state. The dichotomy in MW susceptibility between two strains congenic at the H-2-Tla region on chromosome 17 (AKR-responder and 3.6-H-2k) confirmed the noninvolvement of the Crl-1 gene and indicated that the essential gene was located outside the H-2 region. The strain distribution of MW responsiveness in the BXH RI lines demonstrated that the MW-induced increase in CRL was controlled by a single regulatory gene located on chromosome 5. MW responsiveness was studied in two congenic strains of mice which possess different C3H/HeJ segments of chromosome 5 inserted into a C57BL/6J background. The JG3F/LeTy strain exhibited an increase in CRL indicating possession of the segment of C3H/HeJ chromosome 5 that controls MW responsive-

ness. The C57BL/bJTy-1e strain remained nonresponsive. This places the essential regulatory gene to the right of the PgM-1 locus and to the left of the rd locus on chromosome 5. The data confirm the genetic control of the transitory increase in CRL frequency induced by a single exposure to 1450 MHz radiation and demonstrate that genetic control was due to a single regulatory gene that was functional in the heterozygous as well as the homozygous state.

0393 A GENERALIZED MODEL FOR THE INTERACTION OF MICROWAVE RADIATION WITH BOUND WATER IN BIOLOGICAL MATERIAL. (Eng.) McClean, V. E. R. (Physics Dept., Queen Elizabeth Coll., London W8 7AH, England); Sheppard, R. J.; Grant, E. H. *J Microwave Power* 16(1):1-7; 1981 (17 refs).

Calculations of the deposition of microwave (MW) energy in bound water surrounding a biological macromolecule are based on a previous model of a hydrated macromolecule consisting of a spherical core surrounded by a concentric shell of bound water immersed in a continuum of free water with dissolved ions. Ideally the dielectric properties of the bound water would be considered to vary smoothly across the shell, ranging from the water most tightly bound to the relaxation time of free water; however, to facilitate the calculations, the change is considered to take place in 5 steps for most cases. The average energy deposited per unit volume of the bound water shell was calculated from 100 MHz to 10 GHz for various assumed relaxation frequencies. Sub-shells were assigned the following frequencies: 100-900 MHz in increments of 200; 5-50,000 MHz in multiples of 10; a homogeneous layer of bound water of relaxation frequency 500 MHz; 1000-9000 MHz in increments of 2000; 10-90 MHz in increments of 20; 100-1000 MHz in increments of 100; and free water with a relaxation frequency of 26 GHz. The calculations were carried out for a low value of ionic conductivity of 0.001 S/m for both the free and the bound water. Calculations were also carried out for the first three cases (all which assume a central relaxation frequency of 500 MHz) for conductivities of 1 S/m. At equal but low conductivities, MW energy deposition was greater in bound water (sometimes by at least one order of magnitude) than in free water at frequencies of a few hundred MHz to a few GHz. This effect decreased with increases in ionic conductivity; and at conductivities equal to those of physiological saline, specific energy deposition in bound water was no more than twice that in the electrolyte continuum over the same frequency range. The results show that the biological effect of MW radiation at a given power density is enhanced in tissues with a high bound water content. For tissues of high ionic conductivity and containing 20% bound water, overall energy absorption would be 25% greater at certain frequencies than if all the water were in the free state. For tissues of low ionic conductivity, the increase would be more than one order of magnitude.

0394 EVIDENCE FOR MICROWAVE-INDUCED ACOUSTICAL RESONANCES IN BIOLOGICAL MATERIAL. (Eng.) Olsen, R. G. (Naval Aerospace Medical Res. Lab., Pensacola, FL 32508); Hammer, W. G. *J Microwave Power* 16(3&4):263-269; 1981 (7 refs).

Resonant stress waves were induced by microwave (MW) energy in two biological models: a rectangular muscle equivalent mass of 15 kg and a spherical brain equivalent model of 5 cm radius. The rectangular muscle model was irradiated using a horn antenna at 5.655 GHz energy with a peak power of 200 kW and pulse separation of 380 usec. Pulses were repeated to produce reinforcing. The spherical model was irradiated by single pulses or short bursts of 1.10 GHz energy with peak power of 4 kW and pulse durations of 10-50 usec. Stress waves were monitored by hydrophone transducers at the center of each model. In the rectangular model the amplitude of the induced stress wave was 3-fold greater for four properly spaced radiofrequency pulses than for a single pulse. In the spherical model a single pulse of energy produced a resonant response which decayed exponentially with a time constant of about 500 usec. A burst of three pulses induced stress waves of greater peak amplitude than those induced by a single pulse. A burst frequency of 16 kHz generated the largest effect with a doubling of the amplitude of the induced stress waves compared to that from a single pulse. These experiments showed the importance of pulse width and pulse repetition rate in the generation of sonic energy in biological materials with MW energy. The specific absorption rates in the spherical model were determined calorimetrically to be 824 W/kg at the center and 653 W/kg at the surface closest to the MW source.

0395 LOCAL HYPERTHERMIA USING MICROWAVES FOR THERAPEUTIC PURPOSES - EXPERIMENTAL STUDIES OF VARIOUS APPLICATIONS. (Eng.) Guerquin-Kern, J. L. (Lab. Thermologie Biomedicale, Faculte de Medicine 11, rue Humann, 67085 Strasbourg Cedex, France); Palas, L.; Priou, A.; Gautherie, M. *J Microwave Power* 16(3&4):305-311; 1981 (5 refs).

The electromagnetic heating of biological tissue was studied using physical models and infrared liquid crystal, or thermistor probe thermography. A preliminary study was also reported in which the transient heating of a one-dimensional tissue slab is calculated subsequent to heating by 2,450 MHz or 434 MHz plane wave radiator. The models consisted of excised adipose and muscular tissue from animals, human adipose tissue from a surgical procedure, and phantoms composed of a gel and a polyester resin to simulate adipose and muscle tissue. The effects of surface cooling and use of multiple apertures on the heating pattern were examined using these models and two types of applicators operating at 2,450 and 434 MHz. The experimental results are consistent with the calculated values and demonstrate the need for surface cooling and the advantage of a "cross-fire" configura-

ation in producing local hyperthermia.

0396 TEMPERATURE PROFILES IN SPHERES DUE TO ELECTROMAGNETIC HEATING. (Eng.) Kritikos, H. N. (Dept. Electrical Engineering, Univ. Pennsylvania, Philadelphia, PA 19104); Foster, K. R.; Schwan, H. P. *J Microwave Power* 16(3&4):327-344; 1981. (33 refs).

The steady state temperature increase in a tissue sphere (modeling the human head) irradiated by plane wave microwave energy was estimated for different frequency regions. The heat transport in the tissue was modeled by a differential equation to include heat conduction, heat convection by blood flow and heat transport from the tissue surface into space. For each frequency range, the heat transport equation was solved using an analytic approximation of the heating potential. The steady state increase in tissue temperature and the specific absorption rate (SAR) are plotted as functions of distance from the center of the sphere. The steady state temperature increase resembles the SAR but, for physiologically reasonable values of blood flow, the temperature increases are averaged over approximately 1 cm. The convection length is defined as a function of blood flow. This quantity estimates the distance over which temperature variations occur and allows for an approximation of the distance over which the fine structure of the SAR may be averaged. The maximum steady state temperature increase and its location are summarized for each frequency range and a field intensity of 10 mW/cm². For frequencies less than 500 MHz and a sphere radius of about 10 cm, the maximum steady state temperature increase is less than 0.03 C and is located close to the front surface of the sphere. For frequencies less than 500 MHz and a sphere radius of about 5 cm, no significant temperature is produced. For frequencies of around 1 GHz and a sphere radius of 5 cm, the maximum steady state temperature increase is 0.6 C and is located at the center of the sphere. For frequencies above 5 GHz, only surface heating is produced. The maximum steady state temperature is produced at the front surface of the sphere and is about 0.3 C.

0397 MICROWAVE AND RF HAZARD STANDARD CONSIDERATIONS. (Eng.) Schwan, H. P. (Dept. Bioengineering, Univ. Pennsylvania, Philadelphia, PA 19104). *J Microwave Power* 17(1):1-9; 1982 (49 refs).

Microwave (MW) and radiofrequency exposure safety hazards are reviewed. Considerations for establishing a 10 mW/cm² standard for MW radiation are outlined. Recent results are surveyed and basic mechanisms and appropriate exposure limits examined for four frequency ranges: below resonance, resonance, hot spot, and surface heating. Below several hundred MHz, hu-

man bodies can resonate with electric fields. A maximum average specific absorption rate (SAR) occurs around 30 MHz for man. In the resonance range, the absorption can quadruple if the direction of the electric field is parallel to the long axis of the body. An exposure standard of less than 10 mW/cm² is necessary in this frequency region. Above the resonance range to about 3 GHz, hot spots may be produced in portions of the body. Temperature elevations in the head of up to 0.5 C at power densities of 10 mW/cm² have been predicted from numerical calculations. For frequencies below the resonance range (< 30 MHz) and above the hot spot range (> 3 GHz), only surface heating is produced. The 10 mW/cm² standard provides a safe margin for these frequencies. Tolerable heat loads are functions of environmental conditions as well as of incident radiation intensity and exposure time. Recent studies support a time constant of 0.1 hr as the limit separating short and long term exposures.

0398 THE DEVELOPMENT OF MICROWAVE POWER APPLICATIONS IN CHINA. (Eng.) Chen, H.-K. (Microwave Res. Lab., E. China Normal Univ., Shanghai, China); Shen, Z.-Y.; Fu, C.-S.; Wu, D. *J Microwave Power* 17(1):11-15; 1982 (3 refs).

Applications of microwave (MW) power in China have increased gradually since China began manufacturing continuous wave (CW) magnetrons in 1973. The largest CW magnetrons made in China are 10 kW at 2450 MHz and 30 kW at 915 MHz. Principal applications are MW heating in food processing, timber drying, paper drying, magnetic tape drying, and drying of traditional Chinese medicines. Thermotherapy research, with emphasis on combining local MW heating with cancer chemotherapy or radiotherapy, is being conducted in several hospitals. Other research areas include the combination of MW therapy at 1000 MHz and traditional acupuncture, male birth control, silkworm breeding, and plant germination (using 3-cm, 30-cm, and 1-m MW). Theoretical work has involved box-type MW applicators, uniformity of temperature distribution in applicators and improvement of magnetron performance. In 1978, the following standards were recommended in China: a power density of 50 uW/cm² (6 hr/day) as the provisional safety standard for MW exposure and 300 uW/cm² as the maximum allowable dosage per day.

0399 ERROR SOURCES AFFECTING THERMOCOUPLE THERMOMETRY IN RF ELECTROMAGNETIC FIELDS. (Eng.) Chakraborty, D. P. (Dept. Radiation Oncology, Univ. Alabama in Birmingham, Birmingham, AL 35233); Brezovich, I. A. *J Microwave Power* 17(1):17-28; 1982 (20 refs).

The errors resulting from use of thermocouples for measuring temperature in the presence of the radio-

frequency (RF) electromagnetic fields used for clinical hyperthermia are analyzed. RF currents capacitively or inductively coupled into the thermocouple-detector circuit produce incorrect temperature readings called "pick-up" errors as well as errors due to RF heating at the junction of the thermocouple. A filter between the thermocouple and detector and an aluminum foil shield around the detector eliminate the pick-up errors. The heating effects at the thermocouple junction were divided into three categories: junction current heating, tissue heating, and eddy current heating. The magnitude of each error was estimated and necessary conditions for minimizing errors were outlined. At 13.56 MHz and voltage levels below 100 V rms, errors are shown to be less than 0.1 °C if the thermocouple is properly insulated and recommendations for reducing error are followed.

0400 PECAN WEEVIL CONTROL BY DIELECTRIC HEATING. (Eng.) Nelson, S. O. (U. S. Dept. Agricultural Res. Service, Richard B. Russell Agricultural Res. Center, Athens, GA 30613); Payne, J. A. *J Microwave Power* 17(1):51-55; 1982 (13 refs).

The use of 43 or 2450 MHz electromagnetic energy was examined for killing pecan weevil larvae in intact pecans or in pecan pieces. Samples were irradiated for various periods between the parallel plates of a power oscillator at 40 or 43 MHz with an average electric field intensity of 1.0 or 1.3 kV/cm or in a microwave oven operating at 2450 MHz with 800 W total power output. The temperatures were measured immediately after exposure. Pecan weevil larvae in intact pecans were all killed after 25 sec of parallel plate exposure at 40 MHz after which the temperature of the pecans was 62 °C. Germination of the pecans with a 3% moisture content was not significantly reduced by 43 MHz treatment until the kernels were heated to 50 °C; a temperature of 75 °C completely prevented germination. The differences in moisture content for the whole pecans and the pecan pieces and its effect on heat conductivity and larvae mortality are discussed.

0401 MICROWAVE THERMOGRAPHY - CHARACTERISTICS OF WAVEGUIDE APPLICATORS AND SIGNATURES OF THERMAL STRUCTURES. (Eng.) Robillard, M. (Centre Hyperfréquences et Semiconducteurs, Univ. Sciences et Techniques de Lille I., B t P4, UER IEEA, 59655 Villeneuve, D'ASCQ Cedex, France); Chive, M.; Leroy, Y.; Audet, J.; Pichot, C.; Bolomey, J. C. *J Microwave Power* 17(2):97-105; 1982 (29 refs).

A method based on the antenna reciprocity principle permits computation of thermal signals emitted by biological tissues measured by microwave (MW) thermography. The computation requires knowledge of the temperature distribution and the electrical field distribution in the lossy medium when the probe, or applica-

tor, is radiating a MW signal. Computed thermal signals were verified in experiments with a MW radiometer including a low noise preamplifier, a heterodyne receiver, and a microprocessor for numerical filtering, operating at a central frequency of 3.2 GHz and bandwidth 1.0 GHz. The resultant data can be considered as thermal signatures of a given thermal structure which is defined by a set of parameters describing its shape, position, depth, and temperature. Quantitative determination of temperature distribution in tissues can be obtained if experimental and computed thermal signatures are identical.

0402 OBSERVATIONS OF SYRIAN HAMSTER FETUSES AFTER EXPOSURE TO 2450-MHz MICROWAVES. (Eng.) Berman, B. (EPA, MD74C, Res. Triangle Pk, NC 27711); Carter, H. B.; House, D. *J Microwave Power* 17(2):107-112; 1982 (11 refs).

The teratogenic potential of microwave (MW) radiation was investigated in Syrian hamsters exposed to 2450 MHz continuous wave MW energy (power densities of 20 or 30 mW/cm²) for 100 min/day on gestation days 6-14. Exposure to 20 mW/cm² at a specific absorption rate (SAR) of 6 mW/g caused no significant changes in fetal survival, body wt, or skeletal maturity. Exposure to 30 mW/cm² (SAR of 9 mW/g) resulted in significant increases in fetal resorption and in decreases in body wt and skeletal maturity. Incidences of major and minor anomalies in the two exposure groups did not differ significantly. After exposure to 20 mW/cm² and 30 mW/cm², rectal temperatures of pregnant hamsters increased 0.4 °C and 1.6 °C, respectively, over those of sham irradiated dams. However, maternal toxicity was not observed at either exposure even though maternal rectal temperatures rose to almost 40 °C at 30 mW/cm². Thus, the loss of body wt observed in fetuses irradiated at 30 mW/cm² was not secondary to general maternal toxicity. Fetotoxic effects of MW irradiation were compared in mice and hamsters. In mice, decreased fetal body wt and skeletal immaturity were not observed at an SAR lower than 16 or 22 mW/g. In hamsters, an SAR of 9 mW/g causes similar changes and also causes a significant increase in fetal death (resorptions). The results suggest that the hamster fetus is more susceptible to MW radiation than the mouse fetus.

0403 ASSESSMENT OF IMMUNE FUNCTION DEVELOPMENT IN MICE IRRADIATED IN UTERO WITH 2450-MHz MICROWAVES. (Eng.) Smialowicz, R. J. (Immunobiology Section, Cellular Biophysics Branch, Health Effects Res. Lab., EPA, Res. Triangle Pk, NC 27711); Riddle, M. M.; Rogers, R. R.; Stott, G. A. *J Microwave Power* 17(2):121-126; 1982 (17 refs).

Immune responses at age 3 and 6 wk were studied in male mice born to time-bred CD-1 mice irradiated with

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2,450-MHz microwaves (MW) at an incident power density of 28 mW/cm² for 100 min/day from day 6 to day 18 of pregnancy. The average specific absorption rate (SAR) was 16.5 W/kg, more than twice the basic metabolic rate of the mouse. In contrast to recent reports of MW-induced stunting in mice, no consistent growth retardation was observed. Primary antibody responses to sheep red blood cells (SRBC) were similar in irradiated and sham-irradiated mice. There was also no difference in hemagglutination or hemolysis titers to SRBC. In utero MW exposure did not increase blastogenic responses of T or B lymphocytes to mitogens. Natural killer (NK) cell activity against YAC lymphoma cells was reduced in 6-wk-old mice, but there was considerable variability in NK activity among mice in a given group. Differences in NK activity between irradiated and control mice were not marked. Further studies are needed to corroborate growth-retarding effects of MW exposure and to determine whether neonatal stunting is related to impaired development of NK cell activity.

0404 COAXIAL NONMETALLIC THERMOCOUPLE WITH ELECTRONIC ICE POINT FOR DOSIMETRIC USE IN ELECTROMAGNETIC ENVIRONMENTS. (Eng.) Olsen, R. G. (Naval Aerospace Medical Res. Lab., Pensacola, FL 32598); Hammer, W. C.; Taylor, J. C. J Microwave Power 17(2):137-143; 1982 (11 refs).

An improved nonmetallic thermocouple (NMT) that can provide multiple simultaneous temperature measurements in irradiated subjects at modest cost is described. The NMT is relatively non-perturbing, stable, and linear in output in microwave (MW) environments. The temperature sensitive portion of the coaxial NMT is the tip junction between a carbon-bearing fluorocarbon wire and an outer coating of conductive elastomer. A slightly modified, commercially available electronic ice point provides compensation for the effects of changes in ambient temperature. Specific absorption rates (SAR) measured by the NMT and the more sophisticated Vitek probe in tissue-equivalent material were compared in two MW irradiation tests. A 6-cm diameter muscle-equivalent sphere was exposed for 60-300 sec periods to 5.655 GHz MW energy produced by a military type radar transmitter with a peak output power of 200 kW (0.5 usec pulses at 240 pulses/sec). A 4-kg mass of muscle-equivalent material was placed in a large MW irradiation chamber and exposed in the far field of a horn antenna to continuous wave 2.4 GHz MW energy generated by a Singer 6600 sweeper/oscillator and amplified to 300 W by a MCL Model 10270 Klystron. Essentially no difference was seen in the SAR determined by either probe at 5.655 GHz. At 2.4 GHz, a small difference was seen which was probably the result of the two probes being slightly misplaced during irradiation. The results show that the coaxial NMT offers a useful alternative to more sophisticated and costly temperature probes in certain MW dosimetric configurations.

0405 EFFECTS OF AMBIENT TEMPERATURE AND EXPOSURE TO 2,450-MHz MICROWAVE RADIATION EVAPORATIVE HEAT LOSS IN THE MOUSE. (Eng.) Gordon, C. J. (Bio-engineering Branch, Experimental Biology Div., Health Effects Res. Lab., EPA, Res. Triangle Park, NC 27711). J Microwave Power 17(2):145-150; 1982 (25 refs).

Effects of ambient temperature and microwave (MW) exposure on physiologic heat dissipation were studied in 4 mo old male CBA/J mice. Whole-body evaporative heat loss (EHL) was measured as whole-body evaporative water loss (EWL) in mice exposed individually to continuous wave 2,450 MHz MW radiation for 90 min and an ambient temperature of 20 C and in nonexposed mice maintained at ambient temperatures of 20-35 C. The ambient temperature threshold for increasing EWL was 30-33 C. At an ambient temperature of 20 C, a specific absorption rate (SAR) of 29 W/kg was required for a significant increase in EHL. Above 29 W/kg, a linear elevation in EHL was seen with increasing SAR. The mouse dissipated 65% of the total absorbed heat by water evaporation; the remainder was dissipated passively. Extrapolation of a threshold SAR in a laboratory animal to man necessitates a logarithmic scaling factor. Thus, a SAR of 29 W/kg in a 0.0034-kg mouse is equivalent to an SAR of 0.25 W/kg in a 70-kg man.

0406 TWO-DIMENSIONAL TECHNIQUE TO CALCULATE THE EM POWER DEPOSITION PATTERN IN THE HUMAN BODY. (Eng.) Iskander, M. F. (Dept. Electrical Engineering, Univ. Utah, Salt Lake City, UT 84112); Turner, P. F.; DuBow, J. B.; Kao, J. J. J Microwave Power 17(3):175-185; 1982 (15 refs).

A numerical procedure using the method of moments to determine the heating patterns in two-dimensional models of human cross sections irradiated by aperture sources is described. X-ray computerized axial tomographic scans are used to determine the size, shape, and location of internal tissues for the two-dimensional model. The incident electric field is assumed to be directed perpendicularly to the cross sectional area and to be a half wavelength cosine function with its maximum at the aperture center. The cross-sectional model is divided into cells of a size < 1/10 of the wavelength inside the dielectric. The size of each cell was chosen according to the permittivity of the tissue; it was smaller for high permittivity tissues (heart and muscle) and larger for low permittivity tissues (bone, fat and lung). The electric field and power density distribution at 70 MHz is shown for a human thorax divided into 201 cells and irradiated by eight aperture sources in an annular array. High power deposition is shown in the central area where the heart is located. Experimentally measured temperature increases in a homogeneous tissue phantom exposed to over 1,000 W for 10 min and a sacrificed pig exposed to 1,500 W for 10 min agreed with theoretical results from the two-dimensional model.

0407 AN EMPIRICAL TIME-INTENSITY RELATIONSHIP FOR THERMAL BIOELECTROMAGNETIC EFFECTS.
(Eng.) Miller, T. M. (Dept. Civil Engineering, Northwestern Univ., Evanston, IL 60201); Brodwin, M. E.; Cember, H. J Microwave Power 17(3):195-202; 1982 (26 refs).

An empirical formula relating the exposure time needed to induce a biological effect to the specific absorption rate (SAR) was based on an analysis of published experimental data on laboratory animals and on pain threshold studies on humans. The bioelectromagnetic effects considered were lethality, cataractogenesis and threshold pain sensation in a frequency range from 2.45 GHz to that of visible light. For each effect, a critical organ was chosen as the anatomical location where absorbed radiation produces the specific effect. The critical organs for lethality, cataractogenesis, and threshold pain are the whole body, the crystalline lens of the eye, and skin, respectively. The exposure time needed to induce an effect is reciprocally related to the exposure intensity as measured by the SAR for the critical organ. From regression analysis of each set of data, a general relationship was found giving exposure time as an inverse power function of the SAR. The exponent of the power function is different for each type of experiment. The SAR values of the experimental data ranged from .5 to 4700 W/kg, while the exposure time ranged from 0.25 to 18,000 sec. It is suggested that these empirical relationships may prove useful in representing time-intensity relationships for thermal/harmful biological effects.

0408 RADIOFREQUENCY-INDUCED HYPERTHERMIA IN THE PROSTATE. (Eng.) Scheiblich, J. (Medikon-zept Ltd., PB 1629, D-5190 Stolberg/Rhld., W. Germany); Petrowicz, O. J Microwave Power 17(3):203-209; 1982 (7 refs).

A microwave applicator developed for heat treatment of prostate cancer is described. The 20-mm diameter applicator is insertable into the rectum (insertable length of 175 mm). A high frequency (432.9 MHz, maximum output power, 120 W) slot antenna inside the applicator is cooled with distilled water. To avoid gaps filled with air between the inserted applicator and the rectum, a balloon is filled with water as soon as the applicator is placed correctly. Protective circuits cut off radiation when preselected limiting temperatures (e.g., 41 C on the surface and 46 C in the prostate) are reached. This control system prevents damage to tissue around the prostate, especially the rectal mucosa and tissue between rectum and prostate. Short-term (20 min) and long-term (several treatments in a few wk) experiments were conducted in male dogs at mean power rates of 55 W and 51 W and cooling-liquid temperatures of 2.5 C. Rectoscopic, macroscopic, and micromorphologic examinations showed no damage to the canine rectum, and local heat damage in prostate tissue demonstrating that local hyperther-

mia of the prostate can be achieved safely with the new applicator.

0409 EXPOSURE OF RATS TO 425-MHz (CW) RADIOFREQUENCY RADIATION: EFFECTS ON LYMPHOCYTES.
(Eng.) Smialowicz, R. J. (Experimental Biology Div., Health Effects Res. Lab., Environmental Res. Center, EPA, Res. Triangle Park, NC 27711); Weil, C. M.; Kinn, J. B.; Elder, J. A. J Microwave Power 17(3):211-221; 1982 (31 refs).

The effects of chronic low-level exposure to 425 MHz continuous wave (CW) radiofrequency (RF) radiation on lymphocyte response in rats were studied. Four experiments were performed in which six time-bred pregnant rats were irradiated from day 12 of pregnancy to parturition for 4 hr/day in a temperature controlled exposure system consisting of a rectangular strip transmission line. An AIL 135 power generator capable of supplying 80 W output was used to excite the system. Temperature was maintained at 22 C during irradiation. Four male pups born to each dam were subsequently irradiated under the same conditions for 20-31 or 40-41 days and euthanized. In 3/4 experiments, forward power was 20 W; irradiated dams were inadvertently exposed at 6.6 W forward power in the fourth experiment. In a fifth experiment, pregnant rats were exposed for 16 hr/day from day 5 to day 19 of gestation to 425 MHz CW RF radiation at a forward power of 20 W. Pups were not irradiated. At 22 and 42 days, two pups from each litter were euthanized. No difference was observed in the wt of irradiated compared with sham irradiated rats. Specific absorption rates for rats of different ages derived by twin-well calorimetry or extrapolated from power meter readings ranged from 3.1 to 6.7 mW/g. No consistent change in the peripheral blood picture was observed between irradiated rats and controls. In the first two experiments, a consistently significant increase in the mitogen-stimulated response of lymph node lymphocytes of irradiated rats was observed. The blood lymphocyte response of 40-41 day old irradiated rats displayed an increased response to stimulation by phytohemagglutinin (PHA) as compared with controls in experiments 3 and 4. No change was seen in the hematologic pictures of pups irradiated in utero for 16 hr/day at 22 or 42 days of age. However, node lymphocytes from 42-day-old rats irradiated only in utero incorporated significantly greater amounts of tritiated thymidine than controls following stimulation by PHA and concanavalin A. This increased responsiveness was similar to that seen in rats irradiated both pre- and postnatally. The results suggest that prenatal exposure of rats to 425 MHz RF radiation may be a factor in the lymphoproliferative responses of older rats. The possibility that the increased activity of lymphocytes from irradiated rats was due to a thermally induced stress reaction is noted.

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0410 A RADIO-FREQUENCY MONITOR FOR PROTECTION AGAINST OVEREXPOSURE FROM RF HEATERS. (Eng.) Bini, M. (I.R.O.E., National Research Council, Florence, Italy); Ignesti, A., Millanta, L.; Rubino, N.; Vanni, R. *J Microwave Power* 17(3):223-229; 1982 (5 refs).

A simplified radiofrequency (RF) hazard monitor is described that meets the requirements of isotropy, flat frequency response, simplicity and ease of use, low cost, and includes three indicator lights corresponding to existing safety standards. A green light indicates a field lower than the limit allowed for exposure during an entire working day; a red light indicates a limit beyond which exposure is not permitted; and a yellow light is activated at intermediate levels where part-time exposure is allowed. In the 3-30 MHz band, the monitor has been calibrated to switch from green to yellow at 20 V/m (which corresponds to the USSR standard) and from yellow to red at 150 V/m (which corresponds to a value where 1 min of exposure is allowed in the USA according to ANSI and NIOSH). The limits appear to be compatible with any RF heating machine that is performing reasonably well. The RF monitor has a wide range of potential applications in electromagnetic pollution control.

0411 ULTRASTRUCTURAL CHANGES AND DIFFUSION OF ACETYLCHOLINE IN RAT BRAIN AFTER MICROWAVE IRRADIATION. (Eng.) Kasa, P. (Central Res. Lab., Medical Univ., Szeged, Hungary); Bansaghy, K.; Gulya, K. *J Neurosci Methods* 38(3):749-752; 1982 (10 refs).

Neuron ultrastructure in different regions of the central nervous system was investigated in 9 control and 20 microwave-(MW) irradiated rat brains. CFY rats were sacrificed by decapitation (controls) or by focused high power 2450 MHz MW irradiation to the head for 0.4, 0.8, or 1.0 sec (output power 5 kW, reflected power, 150-150 W). Acetylcholine (ACh) diffusion was examined in cryostat and Vibratome-prepared tissue sections (cortex, striatum, hippocampus, nucleus interpeduncularis, archicerebellum). Little change in neuron ultrastructure was seen after 0.4 sec irradiation. However, the fine structure of neurons was markedly affected by 0.8- and 1.0-sec irradiation. Surface membranes were ruptured and rough endoplasmic reticulum was disorganized in the perikarya. Synaptic vesicles were aggregated, and mitochondria were badly damaged in axon terminals. Cortex and striatum ACh levels were lower in Vibratome than in cryostat sections. This reduction was attributed to diffusion of ACh into the Krebs-Ringer buffer solution.

0412 PULSING ELECTROMAGNETIC FIELD TREATMENT (2 Letters to the Editor). Irvine, R. D. (Hilo, HI); Bassett, C. A. L.; Mitchell, S. W.; Gaston, S. R. *JAMA* 248(8):921; 1982 (1 ref.).

Since most fractures with delayed unions heal spontaneously with time and adequate immobilization, Irvine advocates a double-blind controlled study to evaluate the efficacy of pulsing electromagnetic field (PEMF) treatment described by Bassett et al. [See BENER '71 abstract # 0068]. Bassett et al. point out that 332 of the patients treated with PEMF could not be classed as having delayed union: they had an average disability time of 4.7 yr (range, 2-22 yr) and an average number of 3.4 unsuccessful surgical procedures prior to PEMF treatment; more than one third of these patients were or had been actively infected and at least one recommendation for amputation had been made in 29% of the cases. Of these patients, 75% were healed by PEMFs without further operative intervention. It is agreed that a double blind approach would be useful to fully substantiate claims for PEMF efficacy if sufficient numbers of matched or paired cases can be found for statistical significance to be established; such a study is in progress in the United Kingdom. It is also pointed out that the method is appropriate only for delayed or non-united fractures, as opposed to fresh fractures.

0413 MAGNETIC AND ELECTRIC FIELDS PRODUCED DURING PULSED-MAGNETIC-FIELD THERAPY FOR NON-UNION OF THE TIBIA. (Eng.) Lunt, M. J. (Dept. Medical Electronics, St. Bartholomew's Hosp., London EC1A 7BE, England). *Med Biol Eng Comput* 20(4):501-511; 1982 (13 refs).

A theoretical model is described that can be used to predict magnetic and electric fields produced in bone during pulsed-magnetic-field (PMF) treatment of non-united fractures. The electric field induced by current pulses through two square coils separated by the length of their sides is proportional to the rate of change of magnetic field. A calculation of the charge density at points along the bone/tissue interface indicates that the insulating boundary has modified the field, especially near the coil axis. In the conductor, the field lines circulate; at the insulating surface, they are parallel to the interface. While the model is based on the assumption that bone acts as an insulator it can be extended to allow for the finite resistivity of bone as the effect of resistivity on the surface charge density is small. When a slab of rectangular cross section immersed in a conductor midway between two coils is used as a model of the geometry of bone in tissue, field lines are parallel to the boundary but in opposite directions on each side of the slab; further from the boundary, currents circulate in the tissue, again in opposite directions on each side of the slab. A comparison of theoretical and experimental results (measurements of magnetic fields in air and in tissue, electric fields near a single interface, around a slab, and around a bone) showed good agreement. While the model cannot be used quantitatively to predict the magnitude of the fields produced in a clinical situation, it can predict the effect of changing coil size and separation and can be used to compare the fields from different

current waveforms. The model may also help to elucidate the physical and biochemical mechanisms involved in the healing effects of PMF.

0414 USE OF MICROWAVE TECHNIQUES TO INACTIVATE BRAIN ENZYMES RAPIDLY. (Eng.) Galli, C. (No affiliation given); Racagni, G. *Methods Enzymol* 86: 635-642; 1982 (33 refs).

A technique for sacrificing small laboratory animals using high-intensity microwave (MW) radiation is described, which allows rapid inactivation of metabolic brain enzymes. MW instrumentation has been designed to control the intensity and duration of the incident power and to minimize the reflected power. General specifications are: current, 15 A; power consumption, 3500 W; power output, 1300 W; frequency, 2450 MHz. For adult rats (body wt = 150-300 g), irradiation periods of 2-4 sec are adequate, while for adult mice (body wt = 20-40 g), the values should be 0.7-1.5 sec. For newborn animals the irradiation times should be about 0.5-1.0 sec. The use of focused MW irradiation for animal sacrifice prevents postmortem changes of various neurochemical parameters and gives virtually the same results as the freeze-blowing technique. When samples obtained from animals sacrificed by MW irradiation were compared with those obtained by decapitation, increased levels of cyclic AMP, 3-methoxytyramine, normetanephrine, GABA, and choline and decreased levels of DOPA were seen in the samples obtained by decapitation. Levels of free arachidonic acid (FAA) in brain areas of animals sacrificed by focused MW irradiation were much lower than those measured by decapitation followed by a time interval before analysis; they were not statistically different from levels measured after decapitation and immediate analysis (<30 sec between decapitation and homogenization in organic solvent), or analysis after decapitation and immediate freezing. Levels of prostaglandin (PG) F and thromboxane (Tx), derived through PGH synthase, and HETE, derived through lipoxygenase, were much lower in the brain of animals sacrificed by MW irradiation than in those sacrificed by decapitation followed by a time interval before analysis and were of the same order as those measured in brain tissue frozen in liquid nitrogen immediately after sacrifice. In synthesis, the use of focused MW irradiation prevents both the release of FAA occurring after decapitation followed by a time interval before analysis and the accumulation of PG and Tx observed in the brain even if the interval between decapitation and analysis is less than 30 sec.

0415 ³H-NORADRENALINE RELEASE POTENTIATED IN A CLONAL NERVE CELL LINE BY LOW-INTENSITY PULSED MAGNETIC FIELDS. (Eng.) Dixey, R. (Dept. Medical Electronics, St. Bartholomew's Hosp., West Smithfield, London EC1A 7BE, England); Rein, G. *Nature* 296 (5854):253-256; 1982 (25 refs).

A model system is described for studying effects of extremely low-frequency (ELF) magnetic fields on neuronal functions. Clonal PC12 cells, derived from a transplantable rat pheochromocytoma, were exposed to a pulsing low-frequency magnetic (LFM) field generated between a pair of concentric coils wired in parallel to a pulse pulse generator and driving circuit similar to one used in clinical trials for treatment of non-union fractures. For these experiments, pulse width of 0.6 msec was used with 1.4 msec between each pulse giving an overall frequency of 500 Hz. Maximum and minimum fields applied to the sample were 8.5 G and 1.6 G. Release of ³H-noradrenaline (³H-NA) from PC12 cells was monitored for 12 sequential 15-min periods in 10 trials. Values obtained at 105 and 120 min when cell cultures were exposed for 13 min to LFM fields were always higher than values obtained from the two preceding 15-min time periods. Expressing the stimulated release as the difference between the control and experimental values relative to the control value for a given time period, a stimulation of 27.5% ± 4.9 was obtained for both experimental time periods. In 8 further trials in which 15 mM Mg²⁺ was included in the medium at the 105 and 120 min time periods, the rate of release in control washout curves was not altered, but the stimulated release was abolished. The stimulated release values in the presence of elevated Mg²⁺ were not significantly different from the controls. The results indicate that PC12 cells can be used as a model system for studying the effects of LFM fields on neuronal functions.

0416 DIELECTRIC PROPERTIES OF ANIMAL TISSUES IN VIVO AT RADIO AND MICROWAVE FREQUENCIES: COMPARISON BETWEEN SPECIES. (Eng.) Stuchly, M. A. (Nonionizing Radiation Section, Radiation Protection Bureau, Health and Welfare, Ottawa, Canada); Kraszewski, A.; Stuchly, S. S.; Smith, A. M. *Phys Med Biol* 27(7):927-936; 1982 (17 refs).

An open-ended coaxial line sensor was used to measure the dielectric properties of various tissues of anaesthetised cats and rats at frequencies between 0.1 and 10 GHz. The measurement method is based on determination of the input reflection coefficient of the coaxial line when placed against the test tissue. This coefficient depends on tissue permittivity, frequency, and dimensions of the coaxial line. Dielectric constants and conductivities are reported for skeletal muscle, brain cortex, spleen, and liver and compared with previously published *in vivo* data for cats and rats and for dogs. The differences in the dielectric properties of the same tissue for these species were found to be very small (less than 10%) in the frequency range from 0.1 to 10 GHz, suggesting that lower nonaquatic animals can be used for modeling human beings in developing microwave hyperthermia techniques. At frequencies above 1 GHz, tissue properties correlated well with water content. A comparison of calculated and measured tissue water content indicated that the tissue water in muscle has the dielectric properties of free water while a varied but considerable amount of water in other tissues is in a form of

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bound water.

0417 THE COMPLEX PERMITTIVITY OF HUMAN TISSUE AT MICROWAVE FREQUENCIES. (Eng.) Hey-Shipton, G. L. (c/o Matthews, Dept. Electrical and Electronic Engineering, Leeds Univ., Leeds, Yorkshire, England); Matthews, P. A.; McStay, J. *Phys Med Biol* 27(8):1067-1071; 1982 (8 refs).

The complex permittivity and emissivity of the human body and attenuation coefficient of skin were determined from simple measurements made on living tissue over the frequency range 8 to 18 GHz. The experimental setup consisted of a rectangular waveguide terminated by a semi-infinite flange. The medium inside the waveguide was considered to have a permittivity value identical to that of free space. To create a flat geometry in the plane of the waveguide flange, a plug of expanded polystyrene was inserted into the end of the waveguide. Measurements were made by pushing the waveguide up against the palm of the hand. Power in the waveguide was kept below 10 mW/cm². The VSWR and phase shift of the reflected wave were measured using a precision slotted line, the phase being compared with the reflected wave produced from a flat metal plate pushed up against the flange. The absolute values of VSWR and phase angle for the biological sample were then entered into a computer program whose output gave the value of the complex permittivity of the sample necessary to produce such a VSWR and phase angle. Measurements of real permittivity were about a factor or two lower than those predicted by theory, while the measurements of imaginary permittivity correlated well with existing measured values at about 10 GHz. Emissivity values agreed closely with calculated emissivity values at 8-18 GHz for skin of infinite thickness. Possible sources of error in the measurements of complex permittivity included accurate determination of both VSWR and phase shift, contact of skin with the waveguide flange, and the assumption that the skin could be considered infinitely thick in the area of measurement.

0418 A MICROWAVE HEATING TECHNIQUE FOR THE HYPERHERMIC TREATMENT OF TUMOURS IN THE EYE, ESPECIALLY RETINOBLASTOMA. (Eng.) Lagendijk, J. J. W. (Univ. Hosp. Utrecht, Dept. Radiotherapy, Catharinaesingel 101, 3500 CG Utrecht, The Netherlands). *Phys Med Biol* 27(11):1313-1324; 1982 (12 refs).

A 2450-MHz microwave (MW) stripline applicator for hyperthermic treatment of eye tumors, especially retinoblastoma, is described. The applicator is placed directly on the eye beneath the eyelids so that the geometry can be fixed. The only parameters influencing temperature distribution which cannot be regulated are differences between patients in eye diameter and blood flow. Temperature distributions in human and rabbit

eye resulting from absorbed MW power distribution calculated with a thermal finite difference computer model were verified experimentally on rabbit eyes. Accuracy was better than 0.3 C when the anterior part of the eye was heated to 43-44 C. Accuracy was lower in the posterior half of the eye because of differences in blood flow, but was still better than 0.5 C. Two retinoblastoma patients were treated with x-radiation followed by hyperthermia up to 44 C for 1 hr. Both tumors regressed and no cataracts were induced by MW heating. The complete computer-controlled MW hyperthermia system is described.

0419 MICROWAVE IMAGING OF CEREBRAL EDEMA. (Eng.) Lin, J. C. (Bioengineering Program, Univ. Illinois, Chicago, IL 60680); Clarke, M. J. *Proc IEEE* 70(5):523-524; 1982 (2 refs).

A microwave (MW) transmission technique for detecting and monitoring cerebral edema was demonstrated on a model of the human head. The skull and brain tissue were simulated by a 7.4 cm radius glass sphere filled with 1150 ml of ethanol containing a rubber balloon filled with 550 ml of water to simulate the cerebrospinal fluid. Ethanol and water could be added to or removed from both compartments. A beam of 2.4 GHz MW energy (at a power level <10 uW/cm²) was transmitted through the head model and compared with a reference signal. Relative amplitude and phase were measured by vector voltmeter. The phase change in the MW signal was correlated with changes in fluid volume in the head model. It is shown that volume changes of less than one percent of the total fluid volume could be detected.

0420 A NEW ITERATIVE PROCEDURE TO SOLVE FOR SCATTERING AND ABSORPTION BY DIELECTRIC OBJECTS. (Eng.) Iskander, M. F. (Dept. Electrical Engineering, Univ. Utah, Salt Lake City, UT 84112); Lakhtakia, A.; Durney, C. H. *Proc IEEE* 70(11):1361-1362; 1982 (4 refs).

A new technique, the Iterative Extended Boundary Condition Method (IEBCM), is presented to calculate the scattering and absorption of electromagnetic energy by homogeneous highly conductive dielectric objects. This method increases the solution stability of the Extended Boundary Condition Method which may become unstable at resonant and postresonant frequencies. The IEBCM begins by replacing the lossy dielectric object with a perfect conductor and calculating current densities on the surface; the surface current is used to compute the internal fields inside the dielectric body. The interior of the object is partitioned into overlapping spherical subregions to produce a more efficient convergence. To obtain internal field expansion coefficients, the surface currents obtained from the solution of the external problem are point

matched with the surface currents obtained from the internal expansion, while maintaining the continuity of the magnetic field in the overlapped regions. This procedure yields a zero-order estimate of the internal fields. Further iterations are used to improve the initial estimate of the surface current density. Calculations are presented for the internal field in a spheroidal model of man composed of nine overlapping spheres at 17 MHz.

3421 RADIO-FREQUENCY HAZARDS IN THE VLF TO MF BAND. (Eng.) Gandhi, C. P. (Dept. Electrical Engineering, Univ. Utah, Salt Lake City, UT 84112); Chatterjee, I. Proc IEEE 70(2):1402-1464; 1982 (5 refs).

The external electric (E) fields necessary to generate threshold perception and let-go currents for a human in conductive finger contact with ungrounded metallic bodies (car, station wagon, truck, fence, and roof) were calculated for frequencies from 10 kHz to 10 MHz. The calculated external E-fields for threshold perception were below the proposed ANSI guideline of 100 mW/cm² ($E = 615 \text{ V/m}$ for 0.3 to 3.0 MHz). The human body was modeled as a resistance which varied with frequency and a capacitance which was assumed to be 100 pF at all frequencies. The current through the human body in conductive contact was calculated as a function of resistance, capacitance, frequency, and the short circuit current induced in the metallic object by a vertical E-field. The calculations assume that the E-field lines terminating in the human body and the ungrounded metallic object were not affected by the presence of the other and that object length was smaller than 1/15 or 1/10 of the free space wavelength. Experiments on reduced scale models of a car and a jeep using a 0.1 wavelength monopole-above-ground antenna produced results comparable to the calculated values for a simulated frequency of 0.765 MHz.

3422 STUDIES ON ACUTE IN VIVO EXPOSURE OF RATS TO 2450-MHz MICROWAVE RADIATION. III. BIO-CHEMICAL AND HEMATOLOGIC EFFECTS. (Eng.) Galvin, M. J. (Natl. Inst. Environmental Health Sciences, P.O. Box 12233, Research Triangle Park, NC 27709); Ortner, M. J.; McRee, D. I. Radiat Res 90:558-563; 1982 (22 refs).

The hematologic and biochemical effects of acute microwave (MW) radiation were examined at incident power levels resulting in undetectable thermal stress (as determined by colonic temperature). Male Charles River rats were divided into three groups of 8 animals each (wt = 300 ± 35 g, 10-wk-old) were exposed for 8 hr to continuous wave (CW) 2450 MHz MW radiation in the far field at intensities of 0, 2, and 10 mW/cm² (estimated average specific absorption rates of 0, 0.44, and 2.2 mW/g, respectively). Rats were then de-

capitated, and blood samples were collected for determination of hematocrit, hemoglobin, red blood cell (RBC) and white blood cell (WBC) counts, and differential WBC percentages. No differences in deep colonic temperature, which averaged 38 °C for all three groups, were noted when measured immediately after termination of exposure. Serum levels of protein, beta-glucuronidase, alkaline phosphatase, cholinesterase, and lactic dehydrogenase were not altered by exposure to either MW power density. In addition, MW radiation had no effect on sodium and potassium levels. No changes in the hematocrit or RBC number were noted for either exposure group. There were no differences between the sham and either group of MW-exposed rats in the total number of circulating WBC or percentage of WBC types. It is postulated that the differences in hematologic effects between this study and that found by previous investigators most likely resulted from differences in frequency, mode of delivery (pulsed versus CW), and duration of exposure.

3423 PULSE MICROWAVE EFFECTS ON NERVE VITALITY. (Eng.) McRee, D. I. (Lab. Environmental Biophysics, Natl. Inst. Environmental Health Sciences, P.O. Box 12233, Research Triangle Park, NC 27709); Wachtel, H. Radiat Res 91:212-218; 1982 (9 refs).

The effects of pulsed microwave (MW) radiation on the vitality of frog sciatic nerves were investigated and compared with effects of continuous-wave (CW) MW radiation. Isolated sciatic nerves of frogs (Rana pipiens) were exposed to 2.45-GHz pulse-MW radiation in a waveguide exposure system. In previous studies of CW MW radiation at a specific absorption rate (SAR) of 10 mW/g, survival time of the irradiated nerve stimulated to fire at a high rate (50 twin pulses/sec) was shortened significantly. In this study, 3 sets of experiments were carried out using 10-usec-wide pulses at 50 pulses/sec, with an average SAR of 10 mW/g: (1) asynchronous pulsing wherein the MW pulse was delivered at varying times in the firing cycle; (2) synchronous pulsing during the peak of the nerve action potential; and (3) synchronous pulsing during the quiescent period between nerve firings. In all cases a significant decrease occurred in the survival time of the exposed nerves, as compared with the unexposed nerves. Statistical analysis indicated that the loss of vitality of the exposed nerve was highly significant compared with that of the control nerve. However, the magnitude of this effect was essentially the same in all three cases and was also comparable with the effect seen earlier with CW MW radiation of equivalent SAR. It is suggested that the MW effect on nerve vitality may result from an interference with long-term regulatory processes (such as interfering with maintenance of adequate ionic concentration gradient across the membrane) rather than interference with the mechanism for action potential firing.

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0424 CHANGES IN TUMOR OXYGENATION AFTER LOCALIZED MICROWAVE HEATING. (Eng.) Vaupel, P. (Dept. Physiology, Univ. Mainz, Saarstrasse 21, D-6500 Mainz, W. Germany); Otte, J.; Manz, R. In: Biomedical Thermology. Proceedings of an International Symposium held in Strasbourg, France, June 30-July 4, 1981. Gautherie, M.; Albert, E., eds. (New York: Alan R. Liss, Inc.): pp. 65-74; 1982 (27 refs).

Microwave-(MW) induced changes in tumor oxygenation were investigated by determining the oxyhemoglobin saturation (HbO_2) of single red blood cells within tumor capillaries after MW hyperthermia. Local hyperthermia was induced for 30 min in tumor-bearing Sprague-Dawley rats (270-400 g) of both sexes using 1.5 GHz MW radiation delivered through a special applicator (15 mm outer diameter). Three hyperthermia levels were employed: 40 C, 43 C, and 45 C. Mean tissue temperature for controls was about 35 C. The intracapillary HbO_2 was studied during respiratory normoxia by a cryophotometric micromethod. Upon heating at 40 C, oxygenation of tumor tissue improved significantly ($p < 0.00005$). Directly after 40 C hyperthermia, the mean saturation increased to 66 sat% (median, 70 sat%). However, tumor oxygenation decreased significantly after 43 C hyperthermia compared with control conditions ($p < 0.02$). After a further rise of the mean tumor temperature to 45 C, tumor oxygenation decreased drastically ($p < 0.00005$). The results were thought to reflect changes caused by localized hyperthermia within the tumor tissue itself since no host systemic effects were detected and all tumor biopsies were taken at comparable values of mean arterial blood pressure and of respiratory gas parameters in arterial blood. These results clearly indicate that local hyperthermia has profound effects on tumor tissue oxygenation.

0425 BLOOD FLOW AND TEMPERATURE EVOLUTION OF RHABDOMYOSARCOMA-BEARING MICE DURING NORMAL GROWTH AND DURING SEQUENTIAL HYPERTERMIA TREATMENT. (Eng.) Robert, J. (Lab. Biophysique, Faculte Medicine, 18 rue Lionnois, 54000 Nancy, France); Escanye, J. M.; Marchal, C.; Thouvenot, P. In: Biomedical Thermology. Proceedings of an International Symposium held in Strasbourg, France, June 30-July 4, 1981. Gautherie, M.; Albert, E., eds. (New York: Alan R. Liss, Inc.): pp. 85-95; 1982 (8 refs).

The effects of microwave (MW) induced hyperthermia on tumor blood circulation were investigated in male C3H mice with chemically-induced rhabdomyosarcomas transplanted in the left thigh. Hyperthermia treatment (13 min/day, 5 day/wk for 2 wk) began on day 15 after tumor transplantation when mean tumor size was 1.4 cm and ended on day 29 when mean tumor size was 2.3 cm. Hyperthermia was induced by a 434-MHz MW generator with a high frequency output of 5 W, delivered by a coaxial-type applicator with a contact diameter of 5 mm on the tumor surface. Blood flow and temperature measurements were made on days 15, 23, and 29 after

transplantation. Tumor blood flow, as determined by Venon .33 clearance, decreased when tumor diameter increased. Blood flow in the normal right thigh was comparable to that in the tumor-bearing left thigh when tumor diameter was 1.0-1.5 cm. However, it increased perceptibly as tumor size increased. Rectal temperature and temperature at the tumor surface, at its center, and so in the normal right thigh was recorded. A significant decrease was seen in intratumor and extratumoral temperatures in tumors measuring 1.4-2.0 cm; the decrease was less significant in tumors larger than 2.0 cm. Temperature at the tumor center was about 1 degree higher than at the surface. Rectal temperature was consistently higher than other measured temperatures. Rectal and normal tissue temperature decreased 1.5 C as tumor size increased from 1.4 to 2.0 cm and 0.5 C as tumor size increased from 2.0 to 2.5 cm. The results suggest that the thermoregulatory system of the mice was not altered by MW irradiation of small tumors (diameter = 1.4 cm) while mice bearing big tumors (diameter = 2.0 and 2.5 cm) appeared to loose their thermoregulatory mechanisms. Observed changes are a function of measurement technique, tumor age, existence and extent of previous hyperthermia treatments, and of measurement time.

0426 EFFECTS OF LOCAL MICROWAVE HYPERTERMIA ON LIVER TUMORS: AN EXPERIMENTAL STUDY IN RATS. (Eng.) Hafstrom, L. O. (Dept. Surgery, Univ. Lund, S22185 Lund, Sweden); Hugander, A.; Jonsson, P.-E.; Bolmsjo, M.; Persson, B.; Stenram, U. In: Biomedical Thermology. Proceedings of an International Symposium held in Strasbourg, France, June 30-July 4, 1981. Gautherie, M.; Albert, E., eds. (New York: Alan R. Liss, Inc.): pp. 97-102; 1982 (4 refs.).

An experimental model for local microwave-induced hyperthermic (HT) treatment of liver tumors is presented. Inbred Wistar rats bearing transplanted, chemically-induced hepatic adenocarcinoma were divided by size of tumor into five separate groups that were subdivided into a control group and one subjected to local HT induced by a 2.45 GHz Siemens magnetron radiotherm 305 generator operating at 20 W. The temperature for HT treatment was preset at 41 C. Tumor size was measured 6-8 days after treatment. No difference in growth ratio (size at day of measurement divided by size at day of treatment) was seen in control and treated tumors smaller than 50 mm². Tumors between 50 and 150 mm² treated with HT exhibited a slower growth rate than controls. For tumors between 150 and 200 mm² there was no difference in tumor size between the two groups. Microscopic examination of the tumor-bearing lobe 14 days after local HT revealed an increase in tumor necrosis with increasing tumor size, indicating that the tumoricidal effect of HT was increasing although the difference in tumor size between treated and control tumors decreased. Thus the edema and osmotic effect of necrosis may disguise good tumor response to HT if the response is expressed as change in tumor size.

0427 BIOLOGICAL EFFECTS OF MICROWAVES AND THE QUESTION OF COHERENCE. (Eng.) Frollich, H. (Dept. Physics, The University, P.O. Box 147, Liverpool L69 3BX, England). In: *Biomedical Thermology*. Proceedings of an International Symposium held in Strasbourg, France, June 30-July 4, 1981. Gautherie, M.; Albert, E., eds. (New York: Alan R. Liss, Inc.): pp. 189-195; 1982 (8 refs).

Nonthermal biological effects of microwave (MW) radiation at fields that are weaker than those which give rise to thermal effects and their prediction from theory are discussed. Two possibilities for the trigger action of external electromagnetic waves are presented. One theory refers to coherent electrical vibrations excited by metabolic energy. A small external energy supply may be sufficient to trigger the excitation and the subsequent biological effects. Another refers to a metastable state of large molecules (such as enzymes) with a very high dipole movement. Interaction between the dipoles of activated enzymes may lead to oscillations with a definite frequency and amplitude. This so-called limit cycle may be destroyed by a relatively weak external field with the same frequency thus leading to the liberation of stored energy. In general, frequencies in the second case are much lower than in the first case. The observed nonthermal effects from MW radiation amplitude-modulated at low frequencies may result if the two frequencies work together to yield a stronger biological response than each one individually. This suggests simultaneous application of high and low frequency fields that would arise if the MW energy triggered the excitation of the high frequency vibration while the low frequency acted on the limit cycle. Specific investigations should be performed to determine at which stage in cell development a particular frequency becomes effective. It is speculated that carcinogenesis could occur if foreign chemicals or electrons caused a cell to lose its correct frequency. The vibrational properties of tissues will have to be studied to investigate this speculation.

0428 THERMAL ASPECTS OF BIOLOGIC EFFECTS OF ELECTROMAGNETIC FIELDS AT THE CELLULAR AND MOLECULAR LEVEL. (Eng.) Berteaud, A.-J. (CNRS GR 35, 2 rue Henri Dunant, 94320 Thiais, France). In: *Biomedical Thermology*. Proceedings of an International Symposium held in Strasbourg, France, June 30-July 4, 1981. Gautherie, M.; Albert, E., eds. (New York: Alan R. Liss, Inc.): pp. 197-208; 1982 (20 refs).

Various mechanisms involved in thermal energy transfer into living systems from electromagnetic (EM) fields are reviewed. Cell suspensions have been used to compare the effects of microwave (MW) and conventional heating. Results of studies using zygote formation in *Saccharomyces cerevisiae* to determine global temperature resulting from MW irradiation indicate that heating was due mainly to the dielectric absorption of MW energy by free or loosely bound water molecules

inside the cytoplasm. Thermal stress induced by MW irradiation has been detected by cytoplasmic microviscosity measurements based on fluorescence depolarization. Possible molecular effects of exposure to low-intensity EM fields have been proposed. At radio and MW frequencies, a permanent excitation of metastable states due to thermal noise is present. Long range interactions of EM fields and biomembranes may modify the equilibrium in cooperatively bonded systems existing in periodic structures such as cellular membranes. Direct effects of EM fields on synthetic or natural membranes have been postulated. Mechanisms involved in dielectric losses at radio and MW frequencies are outlined. For water molecules with different chemical bonds at room temperature, dielectric loss can vary as a function of frequency. Heating and thermalization mechanisms in hydrated media such as living matter are discussed. Hydrated water bound to specific biopolymer substrates absorb more energy from incident EM fields than free water regardless of the frequency. Additional research on the mechanisms of interaction of EM radiation with living systems at cellular and molecular levels is needed.

0429 ACTION OF 2.45-GHz MICROWAVES ON THE SYNTHESIS OF PROTEINS IN *SACCHAROMYCES CEREVISIAE*. (Eng.) Dardalhon, M. (Institut Curie, Section Biologique, 26 Rue d'Ulm, Paris 75231, France); Averbeck, D.; Berteaud, A.-J. In: *Biomedical Thermology*. Proceedings of an International Symposium held in Strasbourg, France, June 30-July 4, 1981. Gautherie, M.; Albert, E., eds. (New York: Alan R. Liss, Inc.): pp. 209-218; 1982 (20 refs).

Protein synthesis was examined in yeast exposed to microwave (MW) radiation to investigate the existence of specific thermal effects. The haploid strain N123 of *Saccharomyces cerevisiae* was grown in an anechoic chamber in the presence of MW radiation pulsed every 10 msec at a frequency of 2.45 GHz or in the presence of conventional heating. For MW power levels of 80, 170, 220, 270, 330, and 400 W, incident power values were 10, 20, 30, 40, 50 and 60 mW/cm², respectively. Protein synthesis was determined after treatment at different MW power levels. After 30 min, the rate of protein synthesis (measured by [³H]-leucine incorporation) in MW-irradiated cultures did not differ significantly from that of cultures grown under conventional heating methods. No significant difference was seen in the rate of protein synthesis after 1-hr exposure to either conventional or MW-induced hyperthermia, taking into account a temperature equilibration period of 30 min for the sample. These results, which are consistent with previous findings, suggest that MW action at higher power levels may produce hyperthermia that is not different from that produced by conventional means. The possible contribution of specific MW action to the overall thermic effect was relatively small, if at all present, in these experiments.

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0430 INTERACTIONS OF NONIONIZING RADIATION WITH THE NERVOUS SYSTEM. (Eng.) Albert, E. N. (Dept. Anatomy, George Washington Univ. Medical Center, 2300 I St. N.W., Washington, DC 20037); Sherif, M. F. In: Biomedical Thermology. Proceedings of an International Symposium held in Strasbourg, France, June 30-July 4, 1981. Gautherie, M.; Albert, E., eds. (New York: Alan R. Liss, Inc.): pp. 219-225; 1982 (35 refs).

Literature dealing with the effects of nonionizing electromagnetic radiation (EMR) on the nervous system is reviewed. Russian and Eastern European literature includes reports of a neurasthenic syndrome in individuals occupationally exposed to EMR. Early animal experiments performed to assess the effects of EMR on the nervous system were carried out at high intensities of EMR which resulted in increased body temperature and death. Observed effects could be attributed to thermal stress. However changes have also been reported in the nervous system and brain of experimental animals exposed to lower power densities which appear to be well tolerated and which probably do not produce hyperthermia. Histopathologic changes in the brains of experimental animals subjected to acute exposures to microwave radiation at low power densities (10 and 25 mW/cm²) have been reported. However, unpublished studies showed that chronic exposure to EMR (2450 MHz at 10 mW/cm² for 14 hr/day for 10 wk) did not induce any remarkable morphologic changes in most of the exposed animals. Increased blood-brain barrier permeability has been reported after exposure to EMR at low power density. Most of the research on the effects of EMR on the developing brain has dealt with gross observations on brain. There is very little literature on the effects of low-level EMR on changes in brain cells during development. Similar changes in cerebellar Purkinje cells have been reported after prenatal and neonatal exposure to different EMR frequencies (100 and 2450 MHz) at similar specific absorbed energy levels. The literature in general supports the observation that low-level EMR produces reversible morphologic changes in the nervous system. However, the significance of such morphologic changes is not known at the present time and more research is needed.

0431 IMMUNOLOGICAL RESPONSE OF MAMMALS TO MICROWAVES. (Eng.) Szmigelski, S. (Center for Radiobiology & Radioprotection, 128 Szaserow, 00-909 Warsaw, Poland). In: Biomedical Thermology. Proceedings of an International Symposium held in Strasbourg, France, June 30-July 4, 1981. Gautherie, M.; Albert, E., eds. (New York: Alan R. Liss, Inc.): pp. 227-246; 1982 (42 refs).

Data on the effects of microwave (MW) and radiofrequency (RF) radiation are grouped into the following categories: alterations in immunocompetent cells irradiated *in vitro*; response to low-level, short-term exposure *in vivo*; response to whole-body MW hyperther-

mia; and alterations in natural, nonspecific (antibacterial, antiviral, antineoplastic) resistance in MW-exposed animals. Tabulated experimental data include details of irradiation conditions and periods. The literature does not contain any convincing evidence that metabolic and/or functional alterations occur in immunocompetent cells irradiated in nonthermal MW/RF fields *in vitro*, until thermal effects occur. Short term irradiation of animals in low level and thermogenic MW fields may enhance immune response as evidenced by increased antibody levels, faster maturation of B lymphocytes, and enhanced delayed hypersensitivity reactions. The observed effects are transient and inconsistent and may be explained in terms of nonspecific stress reaction and/or thermal load after irradiation at higher power densities. Long term irradiation in nonthermal MW and RF fields does not provide any convincing evidence for specific immune system response to nonionizing radiation. There may be slight and transient immunosuppression that is not directly related to interaction with MW energy but is explainable in terms of chronic, nonspecific stress reaction. An increase of field power density that is sufficient to increase body temperature by 2 to 3 C evokes distinct responses of hematopoiesis and lymphopoiesis. Results of MW hyperthermia experiments are reported. A biphasic reaction was observed in mice exposed to daily sessions of 2450 MHz MW hyperthermia: stimulation of cell-mediated immunity during the first 4 days of treatment was followed by transient but pronounced immunosuppression. Reduced resistance to staphylococcal infections was observed in mice exposed to low-level or thermal MW fields. Significantly lower clearance of ³²P-labeled staphylococci from peripheral blood of rabbits treated with 2-hr daily sessions of MW hyperthermia was seen. After iv injection of viable cancer cells, mice exposed for 1 to 3 mo to 2450 MHz (2 hr/day, at 5 or 15 mW/cm²) and mice treated with daily sessions of MW hyperthermia for 14 days developed significantly more cancer nodules than controls. Accelerated development of spontaneous breast tumors and 3,4-benzopyrene-induced skin cancer has been reported in MW-irradiated mice. The results suggest that under the tested conditions MW radiation lowers both antibacterial and antineoplastic resistance and that MW radiation may possess cocarcinogenic properties.

0432 INFLUENCE OF THE NEOFORMATION OF BONE TISSUE BY MEANS OF LOW-FREQUENCY PULSED MAGNETIC FIELDS. (Eng.) Haimovici, N. (Dept. Hand Surgery & Operative Rheumatology, Herder Clinic, Am Dobben 103, 2800 Bremen 1, W. Germany). In: Biomedical Thermology. Proceedings of an International Symposium held in Strasbourg, France, June 30-July 4, 1981. Gautherie, M.; Albert, E., eds. (New York: Alan R. Liss, Inc.): pp. 247-255; 1982 (25 refs).

To determine the effect of low-frequency pulsed magnetic fields (PMF) on bone healing, a comparative study was performed in 32 patients with a severe bi-

lateral metatarsus primus varus who underwent simultaneous osteotomies on both feet. The left foot of all the patients (2 male, 30 female; 15-55 yr old) was subjected to two daily PMF treatments (0.5 hr/day for 12 wk; at 10 Hz and 50 G), using low frequency pulsed magnetic field equipment supplied by ELEC. The right foot was not subjected to electrophysical therapies and was shielded from electromagnetic fields. Clinical, radiographic, tomographic and scintigraphic examinations were performed after 1, 2, 4, 6, and 12 mo. The average time for clinical and biologic bone healing was 16 wk for magnetic field-treated cases and 26 wk for the untreated cases. Macroscopically, a solid osseous callus with regenerated bone structure was observed in the magnetic-field treated cases 4 mo after surgery. With the exception of a single case, no complete and definitive bone regeneration was observed in the untreated contralateral feet after the same interval. Microscopic examination revealed that regeneration of the spongy and cortical structure reached a state comparable to normal in most cases treated with PMF. Formation of bone units, stratification, osseous lamellation, ossification, and calcification of the callus were accelerated in PMF-treated cases and improved blood distribution was observed. No temperature increase in joints, bone or adjacent tissue was induced by PMF treatment and there were no signs of irritation or side effects.

0433 HEATING BLOOD IN EXTRACORPORAL CIRCULATION WITH A HIGH-FREQUENCY ELECTROMAGNETIC FIELD: EFFECT OF MICROWAVES ON BLOOD. (Eng.) Andre, J. (Centre de Technologie Biomedicale, INSERM SCN 13, Toulouse, France); Barthelemy, R.; Lefevre, S.; Priou, A.; Morucci, J. P. In: *Biomedical Thermology. Proceedings of an International Symposium held in Strasbourg, France, June 30-July 4, 1981*. Gautherie, M.; Albert, E., eds. (New York: Alan R. Liss, Inc.): pp. 257-268; 1982 (13 refs).

Microwave (MW) blood heating devices are considered as an alternative to the heat exchangers currently used to heat blood during heart surgery and in some cancer treatments using general hyperthermia. The effect of MW heating during extracorporeal circulation (ECC) was studied in 12 40-kg dogs. One group of 6 dogs was treated by conventional techniques for ECC blood heating; a second group of 6 dogs was used for MW blood heating tests. The MW device consisted of a 2450 MHz generator capable of delivering a maximum steady power of 1 kW. The standing wave ratio was 1.02 over a 10-MHz frequency range centered at the working frequency of 2450 MHz. A rectangular waveguide coupled the irradiation cavity to the MW generator. In the conventionally treated dogs, blood temperature was lowered to 29°C at the beginning of the treatment and was returned to 38°C after 30 min by use of a 41°C thermostated bath and maintained at a constant temperature thereafter. In the dogs used for MW blood heating tests, blood was heated to 38°C after being cooled to 32°C (4 dogs) or 29°C (2 dogs). The input power levels (continuous wave) required for

temperature elevation by 6°C and by 9°C were 450 and 650 W, respectively. Blood samples were taken from both groups of dogs at $T_1 = 0$ min, $T_2 = 30$ min and $T_3 = 90$ min; T_1 was taken 20 min after the start of ECC. A fourth blood sample was taken after 5-8 wk. Blood flow rates used for the dogs were about 1000 ml/min. Biochemical and hematologic investigations were carried out. No significant differences between the two heating methods were seen in polynuclear neutrophiles, average globular value, leukocytes, hematocytes, and hemoglobin. No significant variation occurred in metabolic activation during phagocytosis, expressed by the trazolium nitroblue reduction test, or in cell migration capability, measured in the chemotaxis test. Blood biochemical analyses established that no significant differences resulted from either heating method or were found as a function of sampling time.

0434 DIELECTRIC PROPERTIES OF BIOLOGICAL TISSUE. (Eng.) Grant, E. H. (Dept. Physics, Queen Elizabeth Coll., Campden Hill Rd., London W8 7AH, England). In: *Biomedical Thermology. Proceedings of an International Symposium held in Strasbourg, France, June 30-July 4, 1981*. Gautherie, M.; Albert, E., eds. (New York: Alan R. Liss, Inc.): pp. 475-484; 1982 (25 refs).

The motion of ions and the relaxation of water molecules both contribute to the production of heat in biological material which occurs when microwaves (MW) or radio waves are used to treat cancer. The relative contribution of these processes is examined in a discussion of dielectric properties. The four dispersion regions that characterize the dielectric behavior of typical biological material are described and mechanisms of heat dissipation are discussed. At frequencies below the MW region (300 MHz-300 GHz), energy absorption is due mainly to ionic conductivity. However, at MW frequencies, energy dissipation arising from the relaxation of water becomes increasingly important, especially as the water content of most biological tissues is so high. For tissues of high water content, there is nothing to be gained by heating at frequencies higher than 2.45 GHz which can achieve a penetration depth of several cm. However, because of the shortness of wavelength in tissue, 2.45 GHz radiation can produce standing waves in the subcutaneous layers of fat or other tissue, and the maxima of electric field produce localised heating or hot spots. All factors considered, it appears that the optimum frequency for cancer treatment is around 700-900 MHz. The dominant factor determining the energy absorption when MW energy interacts with biological material is the water content. Deposition of energy in free or bulk water and bound water or water of hydration are compared. The dispersion region of bound water occurs at the low-frequency end of the MW region while free water relaxation takes place at frequencies about 10 times greater. Thus bound water is heated differentially at the low-frequency end of the MW region, and tissues with high bound water content will absorb more energy at frequencies from a few ...

MHz up to several GHz than they would absorb if all the water were bulk water. Differential heating of malignant tumors over normal tissue could therefore be achieved over a certain frequency region if malignant tissue had a higher bound water content. Recent studies indicate that malignant tissue has a higher total water content than normal tissue and that the state of water binding may also be different. If the indications can be confirmed by using dielectric methods, it may be possible to identify a frequency region where malignant tissue absorbs more energy than normal tissue.

0435 MICROWAVE RADIOMETRY AND THERMOGRAPHY: PRESENT AND PROSPECTIVE. (Eng.) Leroy, Y. (Centre Hyperfréquences et Semiconducteurs, Lab. Associé au CNRS 287, Université des Sciences et Techniques Lille I, 59655 Villeneuve D'Ascq Cedex, France). In: Biomedical Thermology. Proceedings of an International Symposium held in Strasbourg, France, June 30-July 4, 1981. Gautherie, M.; Albert, E., eds. (New York: Alan R. Liss, Inc.): pp. 485-499; 1982 (80 refs).

A review of microwave (MW) radiometry and thermography is presented. Physical principles underlying MW thermography are summarized and advances in radiometry and thermography are described. Studies of clinical applications of MW thermography undertaken between 1974 and 1980 in the US and France are tabulated. A method to compute thermal patterns based on the antenna reciprocity principle is presented which permits quantification of the subsurface temperature distribution for defined physical conditions (the geometric, thermal, and electrical characteristics of the lossy material, band width of the receiver, and characteristics of the probe) when the probe scans the surface of the lossy material. The use of two (or more) probes to investigate overlapping subvolumes may result in better control over the measurement process. This method is called correlation MW thermography.

0436 MICROWAVE THERMOMETRY IN INTRACRANIAL PATHOLOGY. (Eng.) Thouvenot, P. (Laboratoire de Biophysique, Faculté de Médecine, 18 rue Lionnois, 54000 Nancy, France); Robert, J.; Mamouni, A.; Renard, C. In: Biomedical Thermology. Proceedings of an International Symposium held in Strasbourg, France, June 30-July 4, 1981. Gautherie, M.; Albert, E., eds. (New York: Alan R. Liss, Inc.): pp. 501-508; 1982 (8 refs).

Results obtained by microwave thermometry for imaging intracranial lesions are presented. A radiometer sensitive to 9 GHz and thermographs working at 68, 30, and 11 GHz were used to study 9 healthy subjects and 31 patients with tumors or vascular intracranial lesions. The radiometer was formed by a dielectric loaded waveguide of rectangular cross section (10 x 5 mm) placed perpendicularly in contact with the scalp.

Measurements were made for 13-20 sec at distances of 1-2 cm, 2-4 sec being the theoretical response time. Thermographic measurements were performed at a fixed distance from the scalp unidirectionally and perpendicularly to the sagittal, frontal, or horizontal plane. Recordings were made continuously following sweep lines at a speed of 10-20 cm/min. Results obtained in 9 normal individuals showed good right-left symmetry and absence of sharp variations of local temperatures. Temperatures generally ranged from 34-36°C, the higher values corresponding to the posterior temporal and parietal regions. Of the 31 patients with tumors or vascular lesions, 26 showed the following types of intracranial thermic distribution anomalies: hyperthermia associated with the lesion; hyperthermia associated with the lesion and accompanied by a peripheral hypothermia; hypothermia localized at the lesion; extended hypothermia. No relationship was seen between lesion size and the absence or presence of thermic anomalies. Thermic distribution was modified by 21/22 superficial lesions; however, only 5/9 deep lesions caused any modification. In spite of the high proportion of lesions detected, the radiometry could not be considered as a diagnostic method. The technique seems to be promising for follow-up of lesions and perilesion edemas and for prognostic information on vascular pathology.

0437 THERMOGRAPHIC DETECTION OF HUMAN CANCERS BY MICROWAVE RADIOMETRY. (Eng.) Shaeffer, J. (Radiation Oncology and Biophysics, Eastern Virginia Medical Sch., 600 Gresham Drive, Norfolk, VA 23507); El-Mahdi, A. M.; Carr, K. L. In: Biomedical Thermology. Proceedings of an International Symposium held in Strasbourg, France, June 30-July 4, 1981. Gautherie, M.; Albert, E., eds. (New York: Alan R. Liss, Inc.): pp. 509-521; 1982 (14 refs).

A microwave thermometry system operating at a frequency of 4.7 GHz was evaluated in patients with a variety of biopsy-proven cancers. Temperature differentials consistent with known malignancies were found most often in patients with primary and recurrent breast carcinoma and lymphoma. Little success was realized in detecting more deeply seated tumors which seem to be beyond the detection capabilities of an external antenna.

0438 NEAR-FIELD CHARACTERISTICS OF ANTENNA SENSORS FOR MICROWAVE DIAGNOSIS: PRELIMINARY RESULTS OF MULTISPECTRAL RADIOMETRIC EXPERIMENTS. (Eng.) Edenhofer, P. (Institut für Hoch- und Hochstfrequenztechnik, Univ. Bochum, 463 Bochum 1, W. Germany); Gruner, K.; Steiner, H.; Suss, H. In: Biomedical Thermology. Proceedings of an International Symposium held in Strasbourg, France, June 30-July 4, 1981. Gautherie, M.; Albert, E., eds. (New York: Alan R. Liss, Inc.): pp. 523-537; 1982 (13 refs).

Microwave radiometry is used for remote sensing of spatial temperature distribution in biologic tissue. Broadband antenna sensors are preferred for deriving temperature profiles. Computational results based on a full TE, TM mode analysis are presented for an aperture antenna sensor modeled by an open-ended, rectangular waveguide in direct contact with a multilayer composite biologic tissue (skin-fat-muscle). An undisturbed H₁₀ mode within the aperture plane is assumed. The spacial distribution of power received by the sensor was reduced in penetration depth to values of about 19 mm at 1 GHz and 7 mm at 3 GHz, within the muscle tissue and within the fat layer, respectively. These values in a typical inhomogeneous biologic medium were significantly less than those known for homogeneous plane waves, e.g., at 1 GHz for skin 32 mm (60%) and fat 164 mm (12%). Lateral resolution was about 20% less than the aperture width and exceeded aperture height by 30% at 1 GHz (fat-muscle interface) and by 10% at 3 GHz (within the skin layer). The radiation pattern for an alternative antenna sensor system consisting of an elliptical offset-reflector (distance of foci 1000 mm) and a corrugated horn feed was calculated for 32 and 90 GHz. The power of resolution was 20 mm at 32 GHz and 7 mm at 90 GHz with a focal displacement of 0.75 degrees or 16 mm. Preliminary radiometric images of surface temperature in two test subjects conformed to predicted values.

0439 AN INTERFEROMETRIC METHOD FOR DETERMINING THE ELECTRIC FIELD SCATTERED BY AN OBJECT.
(Eng.) Floyrac, R. (Lab. Biophysique Medicale, Fac. Medicine Grenoble, 38700 La Tronche, France); Dubois, F.; Kom, M.; Baribaud, M.; Bouthinon, M. In: *Biomedical Thermology. Proceedings of an International Symposium held in Strasbourg, France, June 30-July 4, 1981*. Gautherie, M.; Albert, E., eds. (New York: Alan R. Liss, Inc.): pp. 539-545; 1982 (5 refs).

A method to determine the amplitude and the phase of a diffracted electric field which is applicable in microwave imaging is described. This interferometric method is based on the application of the equivalence theorem to Maxwell's equations. In any point in space, the diffracted electric field is the same as the field produced by currents distributed in the illuminated object at a given density. However, the real field that can be measured with a network analyzer is the vectorial sum of the diffracted and incident electric fields which exists at each point when the object has been removed from the incident field. Four measurements are recorded: the intensity of the incident field without the illuminated object, the intensity of the total field with the object, and the intensities obtained by adding the incident field and the total field to the reference field. The time required for the four recordings is about 1 hr.

0440 FLUOROPTIC THERMOMETRY: A NEW RF-IMMUNE TECHNOLOGY. (Eng.) Wickersheim, K. A. (Luxtron Corp., 1960 Terra Bella Ave., Mountain View, CA 94043); Alves, R. V. In: *Biomedical Thermology. Proceedings of an International Symposium held in Strasbourg, France, June 30-July 4, 1981*. Gautherie, M.; Albert, E., eds. (New York: Alan R. Liss, Inc.): pp. 547-554; 1982 (3 refs).

Fluoroptic thermometry is an electrically isolatable, nonperturbing technique for the measurement of temperature in strong radiofrequency (RF) environments using optical sensors. The model 1000A Fluoroptic Thermometer, developed by Luxtron Corp., is a single-probe system designed for use in a variety of laboratory applications. It is small in diameter and available in a choice of lengths, with cabling for extra strength, if required; sterilization of probes by autoclaving appears practical. An absolute accuracy of $\pm 0.1^\circ\text{C}$ is achievable over the biomedical range if a highly conforming (biomedical grade) probe is carefully calibrated before use. A modification of the 1000A for biomedical applications is planned. One or more stable high precision temperature references which can be preset to selected temperatures in the hyperthermia range will be added to the instrumentation system. An optional calibration mode will also be provided. Availability of a multisensor system that allows the use of three to six sensors is expected by late 1982.

0441 THERMAL DOSIMETRY DURING HYPERTHERMIA. (Eng.) Cetas, T. C. (Div. Radiation Oncology, Univ. Arizona Health Sciences Center, Tucson, AZ 85724). In: *Biomedical Thermology. Proceedings of an International Symposium held in Strasbourg, France, June 30-July 4, 1981*. Gautherie, M.; Albert, E., eds. (New York: Alan R. Liss, Inc.): pp. 561-583; (49 refs).

The present clinical status of thermal dosimetry is reviewed. Static phantoms are used for determining power disposition patterns of various heating modalities and applicators. During actual treatment, only a few invasive temperature probes are used to determine subsurface temperatures; surface temperatures are frequently measured with a thermographic camera. Microwave (MW) heating of a surface lesion of melanoma and interstitial thermoradiotherapy of advanced tumors are cited as illustrations of conventional thermometry methods and instruments. Inherent problems with conventional electrical thermometers in the presence of strong electromagnetic fields have led to the development of special thermometer probes designed for use in that environment. Current research activities include investigation of temperature measurement in tumors and surrounding normal tissues by using a non-invasive three-dimensional scanning technique analogous to a computed tomography scan but where the dependent variable is temperature, or by using numerical analysis to compute temperatures everywhere within the

field. Several studies have investigated the application of the Pennes bio-heat equation to thermal dosimetry problems in hyperthermia, e.g., thermal conductivity and power deposition. Volumetric maps of temperature vs time and specific absorption rate vs time would provide information upon which to base thermal dose determinations. Good agreement between experimental and numerical calculations was obtained in a preliminary experiment that involved heating of the thighs of a mini-pig with 915 and 2450 MHz fields. Equipment required for adequate thermal dosimetry includes an automated data-acquisition system that can display information in real time and record it in computer-readable format for later numerical analysis.

0442 EXPERIMENTAL STUDIES OF VARIOUS HEATING PROCEDURES FOR CLINICAL APPLICATION OF LO-CALIZED HYPERHERMIA. (Eng.) Dutreix, J. (Dept. Radiation Therapy, Institut Gustave Roussy, 94805 Villejuif, France); Cosset, J. M.; Salama, A.; Brule, J. M.; Damia, E. In: Biomedical Thermology. Proceedings of an International Symposium held in Strasbourg, France, June 30-July 4, 1981. Gautherie, M.; Albert, E., eds. (New York: Alan R. Liss, Inc.): pp. 585-596; 1982 (27 refs).

The characteristics of various heating procedures that are currently in use are reviewed. Their limitations in clinical hyperthermia are discussed. Thermal contact methods are characterized by superficial heating with a steep temperature gradient. In radiative diathermy, microwave radiation is usually applied as a beam arising from a waveguide; the heat distribution resulting from the beam and its low penetration in tissues is restricted to a small superficial volume corresponding to the central part of the beam. Improvement of the temperature distribution can be achieved using multiple beams. In inductive diathermy, superficial heating is produced by the eddy currents arising in tissues exposed to a high frequency magnetic field. However, tumors with a low blood flow have been heated at depth using a powerful generator operating at 13.5 MHz. In capacitive diathermy, the conventional method of medical diathermy, two flat electrodes are applied on the opposite sides of the region to be treated and supplied with a radiofrequency voltage (usually 27 or 13.5 MHz). Tissues between the electrodes act as a high-loss dielectric in which heat is generated by the electric field. Heat deposition is maximum at the surface under the central region of the electrodes and diminishes at depth and with distance to the axis. Heat distribution is complicated by tissue inhomogeneity. The sc fatty layer is at risk of overheating. In conductive diathermy, heating is produced by local currents passing through tissues between electrodes applied around or implanted within the treated region. For electrodes placed or inserted at a short distance, temperature is fairly uniform in the volume surrounded by the electrodes. Ultrasonic heat deposition in the tissues results from the absorption of ultrasound. Tissue inhomogeneity is a problem. No heating modality currently in use

meets all of the requirements for achieving satisfactory hyperthermia.

0443 DESCRIPTION AND TEST OF A 1.3-GHz MICROWAVE HYPERHERMIA GENERATOR. (Eng.) Escanye, J. M. (Laboratoire de Biophysique, Faculte de Medecine, 18 rue Lionnois, 54000 Nancy, France); Itty, C.; Robert, J. In: Biomedical Thermology. Proceedings of an International Symposium held in Strasbourg, France, June 30-July 4, 1981. Gautherie, M.; Albert, E., eds. (New York: Alan R. Liss, Inc.): pp. 597-604; 1982 (8 refs).

A local hyperthermia system that can be adapted to a previous 434-MHz generator is described. Results of experiments using the apparatus are presented. The apparatus consists of a frequency tripler, amplifier, and applicator. Power input comes from an inexpensive 434 MHz/12 W hybrid communication amplifier and oscillator. The continuous duty cycle power output of the tripler-amplifier unit is 20-25 W at 1.3 GHz applying 600-V anode voltage. The waveguide is entirely filled with dielectric load for compactness and good tissue matching. Experiments on tissue equivalent transparent polyacrylamide gel indicated that the maximum temperature was more than twice as deep at 434 MHz than at 1.3 GHz. A comparison of temperature increases in tumor-bearing mice placed either parallel or perpendicular to the electric field indicated that there is a body shape effect. However, effective penetration depths in tumor-bearing rats were affected principally by vascular and diffusive heat transport.

0444 PRODUCTION AND CONTROL OF 2,450-MHz MICRO-WAVE-INDUCED HYPERHERMIA. (Eng.) Bordure, G. (Centre d'Etudes d'Electronique, Univ. Sciences et Techniques du Languedoc, Place E. Bataillon, 34060 Montpellier Cedex, France); Richard, J. P.; Delauzun, J. P.; Dubois, J. B.; Hay, M. In: Biomedical Thermology. Proceedings of an International Symposium held in Strasbourg, France, June 30-July 4, 1981. Gautherie, M.; Albert, E., eds. (New York: Alan R. Liss, Inc.): pp. 605-610; 1982 (2 refs).

Dogs were exposed to 2450 MHz radiation to determine whether controlled heat can be delivered to a depth of 2 cm without risk to superficial tissue. Hyperthermia was applied with a standard generator fitted with a helicoidal antenna. When theoretical curves for the induction of superficial (0.2 cm) and deep (1.5 cm) temperatures were obtained for two output power levels (100 mW/cm² and 200 mW/cm²), considerable heating of superficial tissue was seen at the higher dose. The curves rose linearly, eventually reaching a steady state. The results of *in vivo* experiments in dogs showed that a relatively small increase in beam strength can lead to a surge in temperature which is difficult to control. Tissue tem-

perature also varied with applicator position. The results suggest that a 2450 MHz source can be used to generate and control hyperthermia for the treatment of superficial and/or deep tumors up to a depth of 2 cm if a precise protocol to modulate output power levels can be defined.

0445 434-MHz MICROWAVE HYPERTHERMIA APPLICATORS: EXPERIMENTAL RESULTS IN PHANTOM AND PRELIMINARY CLINICAL RESULTS. (Eng.) Gaboriaud, G. (Institut Curie, Section Medicale, 26 rue d'Ulm, Paris 75231, France); Jaulerry, C.; Bataini, J. P.; Michel, D.; Dardalhon, M.; Averbeck, D. In: *Biomedical Thermology*. Proceedings of an International Symposium held in Strasbourg, France, June 30-July 4, 1981. Gautherie, M.; Albert, E., eds. (New York: Alan R. Liss, Inc.): pp. 611-620; 1982 (7 refs).

The efficacy of heating with 434-MHz microwaves (MW) was investigated in a phantom and in patients with relatively superficial tumors. A Remy Co. generator (maximum power 100 W) connected to external radiating applicators filled with cooling water was used to induce hyperthermia. MW power was interrupted to perform temperature measurements at sampled intervals. In gel, peak temperature rise was proportional to MW incident power for the same water cooling temperature. Peak temperature rise moved from 0.5 cm to 2.0 cm and the superficial layers were protected from excessive heating when the cooling temperature decreased from 20 to 5°C for the same incident power. Incident MW power must be increased to maintain the same temperature level or to obtain a higher level. Patients presenting with incurable recurrent cancer or with sc metastatic nodules underwent six sessions of hyperthermia alone or in combination with radiotherapy. Sessions were 45 min long with a plateau at 43 to 45°C reached in 2-6 min. There was a large variation of MW power between sessions for the same patients (40-83 W); average temperatures ranged from 40 to 46°C. Tolerance to hyperthermia treatment varied with tumor localization. Partial regression was observed in 3/4 patients treated with hyperthermia alone. Among the 5 patients treated with combined radiotherapy-hyperthermia, one large regression was seen. The results suggest that good hyperthermia at 0.5 to 2.0 cm can be achieved by heating superficial tumors with 434-MHz MW.

0446 434-MHz MICROWAVE GENERATOR FOR LOCALIZED HYPERTHERMIA. (Eng.) Escanye, J. M. (Lab. Biophysique, Faculte de Medecine, 18 rue Lionnois, 54000 Nancy, France); Itty, C.; Robert, J. In: *Biomedical Thermology*. Proceedings of an International Symposium held in Strasbourg, France, June 30-July 4, 1981. Gautherie, M.; Albert, E., eds. (New York: Alan R. Liss, Inc.): pp. 621-626; 1982 (4 refs).

A low-cost microwave hyperthermia system is described

which includes a 16-W -34-MHz generator, a 150-W power amplifier, and a dielectric filled TE₀₁ waveguide applicator. High-frequency power output is increased from 30 to 150 W by switching the high voltage from 600 to 1600 V. A tuner stub is placed between the applicator and the generator. Distance between the skin and the applicator could be increased to 1 cm without affecting the results. In clinical tests, skin temperature was comparable to tumor temperatures at 1 to 2 cm in depth, after an initial 15 min rise, in the no contact condition. Stray radiations did not exceed 30 mW/cm² when the applicator was 1 cm from the skin, at maximum power; 5 mW/cm² was the highest value recorded in a 50 cm radius. Single applicator use limits the system to sc or close-to-skin surface tumor positions.

0447 DEEP AND LOCALIZED HYPERTHERMIA WITH A NEW MICROWAVE SURFACE APPLICATOR. (Eng.) Dittmar, A. (Lab. Thermoregulation L.A. 181 CNRS, Faculte de Medecine Lyon-Nord, 3 Avenue Rockefeller, 69373 Lyon Cedex 2, France); Delhomme, G.; Bourdon, L.; Schmitt, M. In: *Biomedical Thermology*. Proceedings of an International Symposium held in Strasbourg, France, June 30-July 4, 1981. Gautherie, M.; Albert, E., eds. (New York: Alan R. Liss, Inc.): pp. 627-633; 1982 (10 refs).

A direct-contact coaxial applicator developed for use at 2450 MHz is described. The end of the coaxial line is enlarged and shaped like a door knob. The applicator is cooled by water circulating in several circuits that can be monitored separately. Temperature distribution at the applicator surface can be controlled and the amount of heat absorbed by the superficial layers of the model or tissues can be regulated. Temperature measurements were performed in a model consisting of polyacrylamide gel exposed to 2450-MHz microwave (MW) radiation emitted by a magnetron generator with variable power output from 0-200 W. Localized hyperthermias that differed in shape, depth, and intensity were obtained by varying the MW power and the cooling flow in the applicator. Maximal hyperthermia depth of 1 to 4 cm from the surface was determined by the MW power. Surface temperatures did not exceed 36°C with temperatures of 42 or 43°C at depth. The temperature gradient between the maximal hyperthermia and the surface depended on MW power and applicator cooling. Similar results obtained with inert biologic tissues suggest that the applicator is suitable for obtaining focused hyperthermic areas.

0448 A COAXIAL APPLICATOR FOR INTRACAVITARY HYPERTHERMIA OF CARCINOMA OF THE CERVIX. (Eng.) Hand, J. W. (MRC Cyclotron Unit, Hammersmith Hosp., Ducane Rd., London W12 OHS, England); Blake, P. R.; Hopewell, J. W.; Lambert, H. W.; Field, S. B. In: *Biomedical Thermology*. Proceedings of an Internation-

al Symposium held in Strasbourg, France, June 30-July 4, 1981. Gautherie, M.; Albert, E., eds. (New York: Alan R. Liss, Inc.): pp. 635-639; 1982 (7 refs).

A 915-MHz microwave (MW) applicator designed to induce hyperthermia after conventional intracavitary radiotherapy of cervical cancer is described. The complete antenna fits in a conventional cesium after-loading tube (internal diameter, 0.5 cm). Increases in cervical, rectal, and urethral temperatures were measured after insertion of the applicator into the cervix of anesthetized pigs. A MW power level of 10-12 W was required to achieve peak temperatures of 43-44 °C. Temperatures recorded in the rectum and urethra at about 1 cm from the applicator agreed with the radial fall-off in temperature observed in previous liquid phantom studies. No increase in rectal temperature was observed 2 cm from the applicator.

0449 HYPERTHERMIA BY IMPLANTABLE APPLICATORS. (Eng.) Arcangeli, G. (Dept. Radiation Therapy, Istituto Medico e di Ricerca Scientifica, Via S. Stefano Rotondo 6, 00184 Rome, Italy); Barni, E.; Cividalli, A.; Lovisolo, G.; Nervi, C.; Mauro, F. In: Biomedical Thermology. Proceedings of an International Symposium held in Strasbourg, France, June 30-July 4, 1981. Gautherie, M.; Albert, E., eds. (New York: Alan R. Liss, Inc.): pp. 641-647; 1982 (10 refs.).

Thermal dosimetric studies were performed *in vivo* to study the temperature distribution obtained with an implantable applicator operating at 500 MHz. Uniform temperature distribution was obtained in the thigh of an anesthetized lamb with a 5.5-cm applicator and a power ranging from 7-12 W after 20 min heating. The area of therapeutically useful heating had a diameter of approximately 3 cm. Larger areas were heated homogeneously by employing several applicators inserted in different positions at about 3 cm from each other to encompass different tissue shapes and volumes. A new needle applicator has been designed with thermocouples located in the applicator cavity for continuous temperature monitoring and employing a frequency of 1 to 30 MHz.

0450 LOW-FREQUENCY (0.5-MHz) CONTACT AND INTERSTITIAL TECHNIQUES FOR CLINICAL HYPERTHERMIA. (Eng.) Cosset, J. M. (Dept. Radiation Therapy, Inst. Gustave Roussy, 94805 Villejuif, France); Brule, J. M.; Salama, A. M.; Damia, E.; Dutreix, J. In: Biomedical Thermology. Proceedings of an International Symposium held in Strasbourg, France, June 30-July 4, 1981. Gautherie, M.; Albert, E., eds. (New York: Alan R. Liss, Inc.): pp. 649-657; 1982 (3 refs.).

Heating of tissues by low-frequency currents passing between electrodes placed around or inserted into the treated volume was studied. Computed values of the electric field magnitude and current density for maintaining a constant temperature in tissue were in good agreement with values measured in patients. Preliminary clinical results of low-frequency contact and interstitial hyperthermia are presented. Twenty-six patients with intractable superficial metastatic or recurrent tumors were treated with 0.5 MHz techniques; 11/26 were treated with contact electrodes (tubes or plates, usually with water cooling) and 5 were heated with implantation of special needles. A minimum tumor temperature of +1 °C was reached for 15/21 patients treated with contact electrodes and temperatures of 43-44 °C were obtained frequently. Significant hyperthermia was not achieved in 3/21 patients, probably because of the thickness of the fatty tissues under the electrodes. With the interstitial technique, a temperature of about 44 °C was reached easily. Hyperthermia was combined with chemotherapy in 5/26 cases. Analysis of treatment results suggested that a better response was obtained in the patients treated by the interstitial technique and in those who received combined therapy.

0451 E- AND H-FIELD SENSOR SYSTEM. (Eng.) Audone, B. (Equipment Group, Aeritalia, Caselle Torinese, 10072 Torino, Italy); Bolla, L.; Gerbi, G.; Gabriele, P. In: Biomedical Thermology. Proceedings of an International Symposium held in Strasbourg, France, June 30-July 4, 1981. Gautherie, M.; Albert, E., eds. (New York: Alan R. Liss, Inc.): pp. 659-672; 1982 (11 refs.).

Characteristics of electromagnetic (EM) field meters that have been designed, constructed and tested are discussed and tabulated. Sensors in the development phase include instruments that can cover the frequency ranges of 20 Hz to 18 GHz for electric field measurement and 10 Hz to 100 MHz for magnetic field measurement. Design goals include accurate measurement of all polarizations, isotropic probes, balance, and sensitivity to continuous wave as well as modulated field signals. Improvements in repeater units are proposed. A study to improve the accuracy of sensor calibration techniques is underway.

0452 STUDIES ON THE BIOLOGICAL EFFICIENCY OF HYPERTHERMIA PRODUCED BY A MICROWAVE APPLICATOR (434-MHz) FOR THERAPEUTIC MEANS USING AN EUKARYOTIC CELL SYSTEM AS INDICATOR. (Eng.) Dardalhon, M. (Inst. Curie, Section Biologique, 26 Rue d'Ulm, Paris 75231, France); Averbeck, D.; Gaboriaud, G.; Michel, D.; Jaulerry, C.; Bataini, J. P. In: Biomedical Thermology. Proceedings of an International Symposium held in Strasbourg, France, June 30-July 4, 1981. Gautherie, M.; Albert, E., eds. (New York: Alan R. Liss, Inc.): pp. 673-686; 1982 (22 refs.).

The effects of 434-MHz microwave (MW) radiation on biological samples were studied in yeast cells. A MW applicator designed for medical use was filled with water; its surface could be cooled with a thermostated pump-driven water circulation system. The frequency of the 434 MHz generator was stable and the power could be varied from 0 to 100 W. Samples of hyperthermia-sensitive *Saccharomyces cerevisiae* were positioned in a block of muscle tissue in a thermostated water bath and exposed for 1 hr to MW radiation after irradiation with 700 or 1000 Gray (Gy). Results were not significantly different from those obtained with conventional hyperthermia treatment for 1 hr in a thermostated water bath. When the temperature of MW-treated samples was increased gradually, the decrease in cell survival observed was less than with conventional hyperthermia. When the samples were placed in a pre-heated muscle block, rates of cell survival and induction of cytoplasmic "petite" mutations were unaffected by variations in output power or applicator water temperature when sample temperature remained constant and were comparable to those obtained with conventional heat treatment. Cells were maximally sensitized at 1.5-1.8 cm with MW or conventional heating.

Fred von Ardenne, 8051 Dresden, Zeppelinstrasse 7, E. Germany); Kruger, W. In: *Biomedical Thermology. Proceedings of an International Symposium held in Strasbourg, June 30-July 4, 1981*. Gautherie, M.; Albert, E., eds. (New York: Alan R. Liss, Inc.): pp. 705-713; 1982 (28 refs).

The cancer multistep therapy (CMT) concept is based on a combination of hyperthermia and tumor overacidification. Systemic long-term glucose infusion causes a selective drop in tumor pH. The excess glucose contributes to a rise in core temperature through metabolic heat generation which is further elevated by whole-body radiofrequency (RF) heating. The tumor is then heated locally by RF. The limitations of conventional RF heating are overcome by the CMT Selectotherm technique which introduces a movable applicator coil to deliver RF to induce whole-body hyperthermia. After core temperature is elevated to 41°C by scanning the body with high RF amplitudes parallel to the body surface, the RF power is reduced and energy focussed on the tumor area. Target tissue temperatures are 42.5°C. Draining lymph nodes can also be heated locally in a third step, if necessary. Temperature courses during CMT Selectotherm treatment of a patient with inoperable lung sarcoma are shown.

0453 EXPERIENCE WITH DIATHERMIA-INDUCED WHOLE BODY HYPERTHERMIA. (Eng.) Neumann, H. (Dept. Hematology and Oncology, Medizinische Klinik der Albert-Ludwig Univ., Hugstetterstrasse 55, 7800 Freiburg, W. Germany); Fabricius, H. A.; Burmeister, P.; Stahn, R.; von der Tann, M.; Engelhardt, R.; Lohr, G. W. In: *Biomedical Thermology. Proceedings of an International Symposium held in Strasbourg, France, June 30-July 4, 1981*. Gautherie, M.; Albert, E., eds. (New York: Alan R. Liss, Inc.): pp. 697-704; 1982 (24 refs.).

Whole-body hyperthermia was induced in 24 cancer patients with disseminated malignancies using a Siemens diathermy cabinet. Treatment temperatures of 40-41°C were induced by 27 MHz radiation; generator output was 400 W. Chemotherapy was administered iv when a temperature of 40°C was reached. Side effects of cytostatic drugs did not exceed the range observed under nonthermic conditions. An enhancement of metastasis rate was not observed. Changes in hormone levels corresponding to endocrine system response to exercise or stress were observed. Immune parameters that appeared to be affected normalized after treatment; the effects were not correlated with hyperthermia. A patient receiving Adriamycin showed tachyarrhythmia during the fourth hyperthermia treatment, confirming previously reported enhancement of cardiotoxicity of Adriamycin by hyperthermia.

0455 MODERATE-TEMPERATURE WHOLE-BODY HYPERTHERMIA IN THE TREATMENT OF MALIGNANT DISEASE. (Eng.) Wallach, D. F. H. (Dept. Therapeutic Radiology, Tufts-New England Medical Center, 171 Harrison Ave., Boston, MA 02111); Madoc-Jones, H.; Sternick, E. S.; Santoro, J. J.; Curran, B. In: *Biomedical Thermology. Proceedings of an International Symposium held in Strasbourg, France, June 30-July 4, 1981*. Gautherie, M.; Albert, E., eds. (New York: Alan R. Liss, Inc.): pp. 715-720; 1982 (29 refs.).

Results of a Phase I trial of whole-body radiofrequency (RF) hyperthermia at moderate temperature in the treatment of cancer are reported. The hyperthermia unit was constructed after the Siemens prototype. Core heating to 40-41°C was achieved within 30-40 min by deposition of 27-MHz RF energy primarily into the great vessels of the trunk and abdomen. As heating is concentrated in the body core, many physiological compensatory mechanisms are minimized and heating is well tolerated. Nine patients with either disseminated or locally advanced and uncontrollable disease have been treated with hyperthermia 3/wk for 3 wk together with conventional radiotherapy 5 days/wk. Six of these patients completed eight or more courses of hyperthermia. Three patients did not complete their schedule because of complications unrelated to hyperthermia. There were no serious side effects.

0454 COMBINED WHOLE-BODY AND LOCAL HYPERTHERMIA FOR CANCER TREATMENT: CMT SELECTOTHERM TECHNIQUE. (Eng.) von Ardenne, M. (Res. Inst. Man-

0456 LOCALIZED HYPERTHERMIA BY RADIOFREQUENCY WAVES IN THE TREATMENT OF CANCER. (Eng.)

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Israel, L. (Oncology Unit, CHU Avicenne, 125 route de Stalingrad, 93000 Bobigny, France); Besenval, M.; Breau, J. L. In: *Biomedical Thermology. Proceedings of an International Symposium held in Strasbourg, France, June 30-July 4, 1981.* Gautherie, M.; Albert, E., eds. (New York: Alan R. Liss, Inc.): pp. 721-729; 1982 (31 refs).

The differential and preferential thermal sensitivity of malignant tumors and possible mechanisms of action of hyperthermia are discussed. Methods of producing radiofrequency (RF) hyperthermia are reviewed. Results of a phase I-II study of the efficacy of RF hyperthermia in the treatment of large, localized, deep-seated tumors are reported. Fifty-five patients with various deep-seated inoperable, metastatic tumors refractory to conventional treatment were treated by capacitive hyperthermia at 13.56 MHz generated by two soft electrodes. Total heating time ranged from 1 hr to 55 hr; sessions were 45 min to 3 hr long, and patients underwent 1 to 27 sessions. Available energy was increased so that a single field rather than the initial three alternate fields could be used for large tumors. A complete response was seen in 2 patients, a partial response in 15; stabilization for more than 3 mo in 20, and unmodified progressive disease in 18. No systemic toxicity associated with treatment was observed; however, skin burns due to a border effect occurred. It is concluded that localized RF wave hyperthermia is selective, nontoxic, and effective against large, poorly vascularized, deep-seated tumors not responsive to standard therapeutic procedures.

0457 RADIOFREQUENCY THERMOTHERAPY (RFTT) IN THE TREATMENT OF CANCER. (Eng.) LeVeen, H. H. (Dept. Surgery, Medical Univ. South Carolina, 171 Ashley Ave., Charleston, SC 29425); Pontiggia, P. In: *Biomedical Thermology. Proceedings of an International Symposium held in Strasbourg, France, June 30-July 4, 1981.* Gautherie, M.; Albert, E., eds. (New York: Alan R. Liss, Inc.): pp. 731-738; 1982 (7 refs).

A radiofrequency (RF) generator utilizing a frequency of 13.56 MHz and employing multiple portals through which energy is introduced into the body was designed for the treatment of cancer. Multiple electrode pairs are successively energized for brief intervals with constant heating of the tumor, providing penetrating heat without excessive skin heating. The electrodes are refrigerated to further prevent skin overheating. Results obtained in a series of about 60 patients with advanced tumors treated in Italy with RF thermotherapy are reported. RF thermotherapy was effective in the treatment of tumors of different types that were generally in advanced stages; few complications were observed.

0458 SHORTWAVE REGIONAL HYPERTHERMIA OF THE PELVIS. (Eng.) Sidi, J. (Dept. Clinical Der-

matology, Hopital Saint Louis, Place Alfred Fournier, 75110 Paris, France); Jasmin, C.; Convert, G.; Dufour, J.; Azam, G.; Huber, H.; Leger, J. In: *Biomedical Thermology. Proceedings of an International Symposium held in Strasbourg, France, June 30-July 4, 1981.* Gautherie, M.; Albert, E., eds. (New York: Alan R. Liss, Inc.): pp. 739-744; 1982 (3 refs).

An apparatus for shortwave regional hyperthermia of the pelvis is described, and a protocol employed in the treatment of chronic urogenital infections that resist conventional modalities is presented. The apparatus features a three-electrode capacitive heating system and a 1000 W generator operating at 27.17 MHz. Patients with bacteriologically proven chronic urogenital infections were treated every other day for 3 wk; treatment sessions lasted at least 2 hr. Temperatures slightly higher than 41°C were tolerated at the rectal and vaginal level without a significant increase in buccal temperature and with no risk of cutaneous burns. A total generator power of up to 1500 W may be needed for certain patients with a large pelvic volume. Even in cases where treatment could not be completed, a noted painkilling effect was observed. A generator of lower frequency than 27.12 MHz may be used in cases where the patient is resistant to this type of heating.

0459 HYPERTHERMIA FOR HEAD AND NECK MALIGNANT TUMOR. (Eng.) Kijima, T. (Dept. Otolaryngology, Kobe Univ. Sch. Medicine, 7-5-20 Kusunoki-cho, Chuo-ku, Kobe 650, Japan); Hohki, A.; Masuda, M.; Kanatani, K. In: *Biomedical Thermology. Proceedings of an International Symposium held in Strasbourg, France, June 30-July 4, 1981.* Gautherie, M.; Albert, E., eds. (New York: Alan R. Liss, Inc.): pp. 745-749; 1982 (6 refs).

Results are reported in the treatment of 15 patients with head and neck cancer using local radiofrequency (RF) hyperthermia alone (in 2/15 patients), with surgery (1/15), chemotherapy (1/15), radiotherapy (4/15) or combined chemotherapy and radiotherapy (7/15). Hyperthermia was induced by 13.56 MHz RF applied with a surface electrode that could be cooled by circulating cool water. Treatments took place 2/wk. Tumor temperature was controlled between +2 and +5°C. Partial remission was seen in 1/2 patients treated with local hyperthermia alone; complete remission was seen in 1 patient treated with hyperthermia and chemotherapy; 2/4 patients treated with hyperthermia and radiation underwent complete remission; 7 patients treated with combined therapy seem to have responded with complete remission. There was no evidence of central nervous system dysfunction when hyperthermia was applied to nasopharyngeal and mesopharyngeal cancer, and no side effects were reported.

0460 CLINICAL EXPERIENCES WITH COMBINED HYPER-THERMIA AND RADIOTHERAPY IN THE TREATMENT OF CANCER. (Eng.) Friedenthal, E. (Radiotherapy Dept., Montefiore Hosp. and Medical Center, Bronx, NY 10467); Mendecki, J.; Botstein, C.; Sterzer, F.; Pagnione, R.; Nowogrodzki, M. In: *Biomedical Thermology. Proceedings of an International Symposium held in Strasbourg, France, June 30-July 4, 1981.* Gautherie, M.; Albert, E., eds. (New York: Alan R. Liss, Inc.): pp. 751-760; 1982 (12 refs).

Clinical experience with microwave (MW) and radiofrequency (RF) induced hyperthermia at Montefiore Hospital and Medical Center in New York City is summarized. Patients with tumors of various histological characteristics in a variety of stages and anatomical sites have been treated. MW hyperthermia is induced by apparatus operating at 2450 or 915 MHz, which permits heating of tissue up to 2-3 cm in depth. A modified Burdick MW generator and a Mictron 10-W generator are used as the power sources at 2450 MHz and at 915 MHz, respectively. For deeper-seated tumors plane-wave RF heating at 27 MHz is employed. The power source is a Henry Radio generator containing provisions for measuring incident and reflected power. Standardized applicator designs do not exist, and variants of applicators have been developed for particular tumor sites or treatments. Hyperthermia is administered as soon as possible following radiotherapy to ensure higher therapeutic gain (1-hr sessions 2/wk, at 48-72 hr intervals) with tumor temperatures targeted at 42-43°C. In general, no systemic ill effects have been experienced by patients treated with MW-induced hyperthermia. At 27 MHz, control of the heated volume is more difficult, and systemic effects are more pronounced. The effect of heating certain vital organs (e.g., heart, large bowel) must be considered when hyperthermia is applied. Results of treatment in over 100 cases are summarized.

0461 PRELIMINARY RESULTS IN THE TREATMENT OF OAT CELL CARCINOMA OF THE LUNG BY COMBINED AP-PLICATION OF CHEMOTHERAPY (CT) AND WHOLE-BODY HYPER-THERMIA. (Eng.) Engelhardt, R. (Dept. Hematology and Oncology, Medizinische Klinik der Albert-Ludwigs Universitat, Hugstetterstrasse 55, 7800 Freiburg, W. Germany); Neumann, H.; von der Tann, M.; Lohr, G. W. In: *Biomedical Thermology. Proceedings of an International Symposium held in Strasbourg, France, June 30-July 4, 1981.* Gautherie, M.; Albert, E., eds. (New York: Alan R. Liss, Inc.): pp. 761-765; 1982 (12 refs).

Preliminary results are reported for 15 patients with small cell carcinoma (SCC) of the lung treated by multidrug therapy and whole body hyperthermia induced by a Siemens unit. Chemotherapy consisted of Adriamycin and Oncovin administered iv on Day 1 and Cyclophosphamide po on Days 2-5, repeated up to 6 x at 3 wk intervals. Two to five cycles of chemotherapy were administered together with whole body hyperthermia on Day

1; injections of Adriamycin and Oncovin were given at the treatment temperature of $40.4 \pm 0.5^\circ\text{C}$ which was maintained for 1 hr. Complete remission (disappearance of all signs of measurable disease for at least 1 mo) was obtained in 8 patients, partial remission (shrinkage of all measurable tumors by at least 50% for at least 1 mo without new tumor growth) in 5 patients, no change in 1, and progressive disease was observed in 1 patient. Survival rates, calculated from life table analysis, are 87% at 6 mo, 53% at 12 mo, 22% at 18 mo, and 22% at 24 mo. A 50% survival rate is now at 53 wk (12.3 mo). Whole body hyperthermia was well tolerated by the patients. There was no evidence for the acceleration of disease or the stimulation of metastasis by hyperthermia. Given the poor prognosis for patients with SCC (median survival time of 6-8 wk without treatment and 7.6 mo with multidrug therapy), the results are encouraging.

0462 INTRAARTERIAL INFUSION CHEMOTHERAPY IN COM-BINATION WITH 2450-MHz MICROWAVE HYPERTHERMIA FOR CANCER OF THE HEAD OF THE PANCREAS. (Eng.) Miura, T. (Dept. Surgery, Hanzomon Hosp., Tokyo, Japan); Haida, K.; Haida, S.; Wada, T. In: *Biomedical Thermology. Proceedings of an International Symposium held in Strasbourg, June 30-July 4, 1981.* Gautherie, M.; Albert, E., eds. (New York: Alan R. Liss, Inc.): pp. 767-774; 1982 (no refs).

Results of intraarterial infusion chemotherapy in combination with 2450-MHz microwave (MW) hyperthermia in the treatment of 25 patients with advanced cancer of the head of the pancreas are presented. MW radiation was applied to the primary tumor site of each patient for a 10-min period. When the tumor site was heated to a peak local temperature, chemotherapeutic agents were infused through an indwelling catheter in the artery. Of the 25 patients, 17 (68%) survived > 6 mo, and 36% > 1 yr, and 1 patient was alive 46 mo after treatment. These survival rates are uncommon in patients with advanced pancreatic cancer; patients on conventional systemic chemotherapy would have had a 2-3 mo life expectancy. The results indicate that the effects of the intraarterial chemotherapy were potentiated by MW hyperthermia.

0463 MEDICAL USE OF NONIONIZING ELECTROMAGNETIC WAVES IN THE RADIO AND SUPERHIGH FREQUENCY RANGE: HAZARDS AND STANDARDS. (Eng.) Stuchly, M. A. (Radiation Protection Bureau, Health & Welfare Canada, Rm. 233 Environmental Health Centre, Ottawa, Ontario, K1A 0L2 Canada). In: *Biomedical Thermology. Proceedings of an International Symposium held in Strasbourg, France, June 30-July 4, 1981.* Gautherie, M.; Albert, E., eds. (New York: Alan R. Liss, Inc.): pp. 851-865; 1982 (66 refs).

The biophysical basis of the interactions of radiofre-

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quency (RF) and microwave (MW) radiation with living systems is briefly outlined. The sound base of dosimetric data established since the concept of the specific absorption rate was adopted allows better quantification of experimental studies and hazard assessment. Studies investigating thermogenic, genetic, teratogenic, cardiovascular, endocrinological, immunologic, behavioral, auditory, and blood-brain-barrier effects of RF and MW radiation are summarized. Epidemiological studies have failed to produce reliable evidence of detrimental effects of occupational exposure to RF and MW radiation. Exposure levels recommended in both the 1979 Canadian exposure standard and the proposed US standard take into account the dependence of the absorbed dose on frequency. The potential health risk associated with all diagnostic medical applications is small. In hazard assessment for therapeutic uses of RF energy, both the patient and the operator must be considered. Promising medical applications of RF and MW radiation include cancer diagnosis by MW radiometry, NMR imaging, and cancer treatment. Areas requiring further research are outlined.

0464 EFFECT OF LOCALIZED MICROWAVE HYPERTHERMIA ON PHYSIOLOGICAL RESPONSES. (Eng.) Bicher, H. I. (Div. Radiology, Henry Ford Hosp., 2799 W. Grand Blvd., Detroit, MI 48202); Sandhu, T. S.; Vaupel, P.; Hetzel, F. W. Natl Cancer Inst Monogr 61: 217-219; 1982 (21 refs).

Measurements of pH, local blood flow, and tissue oxygen tension (T_pO_2) were performed in normal cat brain and in muscle of the hind leg of C3H Sed-3H mice. Determinations were obtained in both controls and in animals bearing an implanted mammary adenocarcinoma. Modifications in these parameters as a function of temperature and the differential responses observed between normal and tumor tissues were also investigated. Microwave radiation (2,450 MHz) was delivered through a specially-designed applicator loaded with low-loss dielectric material having a dielectric constant of 6. Responses to hyperthermia were similar in both normal tissues except that the temperature at which T_pO_2 began to fall (the breaking point) was significantly lower for the tumor. Blood flow in mice increased significantly up to approximately 41°C. In addition, there was a correlation between decreases in T_pO_2 and blood flow as the temperature was increased to 45°C. The mean value of tissue pH was 6.8 ± 0.2 pH U in C3H mammary tumors. With heating for 1 hr at 43°C, pH decreased 0.5-1 U to 6.2 ± 0.2 . It is concluded that the therapeutic effectiveness of hyperthermia may partially result from several induced physiological modifications: moderate (41°C) hyperthermia in combination with ionizing radiation may result in improved tumor response by increased oxygenation and, hence radiosensitivity coupled with a decrease in tumor pH; hyperthermia at 42°C and above may be directly tumoricidal because tumor micro blood flow is eliminated and tumor pH is sharply reduced, whereas normal tissue is properly perfused.

0465 THERAPEUTIC POTENTIATION OF cis-DICHLORODIAMINEPLATINUM(II) AND RADIATION BY INTERSTITIAL MICROWAVE HYPERTHERMIA IN A MOUSE TUMOR. (Eng.) Douple, E. B. (Norris Cotton Cancer Center, Dartmouth-Hitchcock Medical Center, Hanover, NH 03755); Strohbehn, J. W.; de Sieyes, D. C.; Alborough, D. P.; Trembley, B. S. Natl Cancer Inst Monogr 61: 259-262; 1982 (8 refs).

An interstitial microwave (MW) system for producing local hyperthermia in deep-seated tumors was tested alone and in combination with cis-dichlorodiamineplatinum(II) (cis-PT(II)) chemotherapy and/or radiation in the treatment of mouse mammary tumors implanted in the thighs of C3H/HeJ female mice. A small needle-like coaxial monopole antenna (0.8-cm active length) operating at 1 GHz was inserted into the center of 0.5- to 1.0-cm diameter tumors, and temperatures were monitored and controlled to be either 44 or 45°C maximum at the antenna for 30-45 min. Both MW and conventional heating induced distinct histological changes signifying pyknosis, absence of mitoses, and necrosis. Histological analysis indicated that microwave heating destroyed tumor cells in the center of tumors, whereas water-bath immersion produced cell killing only in the perimeter of the tumor near the skin. Both microwave and water bath heating resulted in severe damage to the legs, i.e., swelling followed by desquamation, necrosis, and eventual leg loss. Compared with water bath heating, less damage to mouse normal leg tissues resulted when microwave heating was used. Analysis of tumor diameter doubling time values for cis-PT(II), radiation, heat, and combination treatments suggests that this method of local heating potentiates the effects of these agents. The results suggest that a single microwave coaxial antenna may serve as an appropriate system for producing local hyperthermia in tumors in small laboratory animals.

0466 FRACTIONATED RADIOTHERAPY AND SHORT-TERM MICROWAVE HYPERTHERMIA. (Eng.) Dietzel, F. (Radiologisches Institut, Städtische Krankenanstalten, 8580 Bayreuth, W. Germany); Lohhart, G.; Grundel, B. R. Natl Cancer Inst Monogr 61: 267-269; 1982 (8 refs).

Experimental groups of 30 to 50 female NMRI mice with solid Erlich neck tumors of 1-ml, were irradiated locally with 5 Gray (Gy) of X-rays followed immediately by localized microwave hyperthermia to 42°C for 3 min. Localized hyperthermia was delivered by a 2,450-MHz Philips generator. Cell loss rate (CLR) was measured by the loss of radioactivity of [^{125}I] deoxyuridine-labeled tumor cells. CLR of hypoxic and oxygenated cells was nearly identical in untreated tumors. Hyperthermia alone had little influence on the loss of oxygenated cells, but it resulted in a significant loss of hypoxic cells. Hyperthermia in combination with irradiation significantly enhanced cell loss of hypoxic cells compared with irradiation alone. For

hypoxic cells, a thermal enhancement ratio of 3.3 and a super-additive factor of 1.22 was obtained. Repeated hyperthermia retarded tumor growth only for a few days, whereas fractionated radiation therapy delayed tumor growth according to the dose applied. With combined treatment, the tumor was under control for the complete treatment time and even for a long period after the last treatment. Eight treatments of 5 Gy each combined with hyperthermia reduced tumor growth more than 8 fractions of 8 Gy alone. Whereas all animals given radiotherapy treatment died before day 100, 13.3% of the animals given the combined hyperthermia treatment survived more than 100 days without recurrence. Whereas 8 Gy given 8 x leads to severe skin reactions, the combination of this amount of radiation with hyperthermia induced almost no skin damage. The thermal enhancement ratio of the fractionated radiotherapy combined with microwave hyperthermia was more than 1.6.

0467 **EFFECTS OF HEAT ON WOUND HEALING IN MICE.** (Eng.) Martinez, A. (Div. Radiation Therapy, Dept. Radiology, Stanford Univ. Sch. Medicine, Stanford, CA 94305), Faria, S. L.; Flores, S.; Hahn, G. M. *Natl Cancer Inst Monogr* 61:307-309; 1982 (7 refs).

The effects of hyperthermia on wound healing in C3H/K mice were studied in order to develop an easy and reproducible model of wound healing; to assess the effects of hyperthermia on wound healing; and to compare the effects of water bath and radiofrequency (RF) heating. Skin and underlying muscle from the right hind thighs of C3H/K male mice, 11-25 wk old, weighing 30-40 g were excised leaving a surgical defect 1 cm in diameter. Five minutes prior to excision, hyperthermia treatments were given at a fixed temperature of 45°C, either in a water bath or with 13.56 MHz radiofrequency, for periods of 10, 20, 30, and 40 min. Microscopic measurements of the excised area were recorded, and the percentage of mice with 50% of the wound healed versus days of follow-up was plotted for analysis. For controls in which an incision was performed without prior hyperthermic treatment, one-half of the mice had 50% of their wounds healed in 8.5 to 9.5 days. In a water-bath control group (temperature kept constant at 37°C) the healing time ranged from 7.5 to 10 days. However, as the water bath temperature was increased to 45°C and kept constant for 10, 20, 30 and 40 min, a delayed healing time was noted as treatment time increased. In the RF group, no significant difference was observed between the control, group treated at 37°C and the mice treated at 45°C.

0468 **INTERSTITIAL THERMORADIOTHERAPY.** (Eng.) Manning, M. R. (Div. Radiation Oncology, Dept. Radiology, Univ. Arizona Health Sciences Center, Tucson, AZ 85724); Cetas, T. C.; Gerner, E. W. *Natl*

Cancer Inst Monogr 61:357-360; 1982 (9 refs).

The results of a phase I clinical trial in which heat was combined with interstitial (low dose rate) radiation are described with emphasis on response and technical and physical aspects of heating. Twenty-five patients (17 lesions) were treated using interstitial implants to locally recurrent, accessible tumors heated by 0.5 MHz radiofrequency currents to 43-45°C for 30 min, with needle guides as electrodes. They were subsequently irradiated with either ¹⁹²Ir or ²²⁶Ra. All patients had failed previous conventional treatments. In all but one, a single hyperthermic treatment was given and the average dose of low dose irradiation was under 3,000 rad over 60 hr. No patient failed to respond, 63% achieved a complete disappearance of tumor in the treated volume, and 37% had partial response (50% <volume reduction<100%). Duration of response varied from 2-30 mo and no patient showed regrowth at the site treated. A cumulative summary of responses based on histology and a comparison of treatment results obtained using heat alone, external heat + external radiation, and interstitial radiation are presented. All but one of the complications observed were considered minimal; the one serious complication was a vaginal-rectal fistula that developed 1 mo after the implant. Other complications including soft tissue vaginal necrosis, fatty liquefaction, and proctitis healed spontaneously. It is concluded that interstitial thermoradiotherapy is both a safe and an effective means of treatment in advanced or recurrent accessible disease. The technique of implantation, subsequent heating, and radioactive after-loading make this procedure applicable to intraoperative approaches in such diseases as unresectable pancreatic carcinoma, tumors of the gastrointestinal tract, and unresectable ovarian disease.

0469 **HYPERTHERMIA EFFECTS IN ANIMALS WITH SPONTANEOUS TUMORS.** (Eng.) Gillette, E. L. (Comparative Oncology Unit, Dept. Radiology & Radiation Biology, Colorado State Univ., Ft. Collins, CO 80523). *Natl Cancer Inst Monogr* 61:361-364; 1982 (12 refs.).

Results of investigators who have used spontaneous canine tumors for evaluation of hyperthermia are reviewed for the purpose of designing appropriate therapeutic protocols for treatment of animal tumors or use of that information as a basis for human cancer therapy.

0470 **MICROWAVE HYPERTHERMIA AND ELECTRON BEAM THERAPY OF SUPERFICIAL TUMORS OF HUMAN ORIGIN IN THE NUDE MOUSE.** (Eng.) Cunningham, D. E. (Dept. Radiology and Specialized Cancer Res. Center, Pennsylvania State Univ. Sch. Medicine, Hershey, PA

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17033); Sharkey, F. E.; Frey, R. A.; Stryker, J. A.; Velkley, D. E. *Natl Cancer Inst Monogr* 61:385-389; 1982 (18 refs).

Seventy-six congenitally homozygous (*nu/nu*) nude NIH Swiss Webster mice were inoculated sc or id with 3×10^7 CMV-Mj-HEL-2, T-1 cells along the dorsal midline. The cells were a strain of human embryo lung fibroblasts transformed in vitro by human cytomegalovirus. Of the superficial tumors that developed after a 19-day latent period, 25 were treated with 2,450-MHz microwave hyperthermia (42.5 C for 20 min) followed by fractionated electron beam therapy (641 rad/fraction) (Group HE); 16 tumors received radiation alone (Group E), 15 received only hyperthermia (Group H), and 15 served as controls (Group C). A 50% or greater reduction in tumor vol occurred in 77% of Group HE tumors, compared with 12% of Group E, 8% of Group H, and 20% of Group C tumors. Complete regression was observed in 50% of Group HE tumors, as opposed to 6% of Group E, 8% of Group H, and 7% of Group C tumors. These results confirm the efficacy of combined heat and radiation treatment in a moderately radioresistant cell line. The results are significant because the cell line is a virally transformed human strain transformed by a human virus; moderately radioresistant in vivo, and in vitro; and not significantly responsive to heat or radiation alone, and demonstrates metastatic capabilities typical of malignant human tumors.

0471 RESPONSE OF SPONTANEOUS ANIMAL TUMORS TO HEAT AND/OR RADIATION: PRELIMINARY RESULTS OF A PHASE III TRIAL. (Eng.) Dewhirst, M. W. (Div. Radiation Oncology, Dept. Radiology, Univ. Arizona Health Sciences Center, Tucson, AZ 85724); Connor, W. G.; Moon, T. E.; Roth, H. B. *Natl Cancer Inst Monogr* 61:395-397; 1982 (10 refs).

Relative differences in control rates and response durations of spontaneous tumors in 13 cats and 41 dogs treated in a phase III randomized trial with heat alone, irradiation alone, or heat plus irradiation are reported. Animals were assigned to three treatment groups and were stratified by histological type of tumor. The histological types treated included melanoma (7), mast cell sarcoma (13), mammary adenocarcinoma (6), fibrosarcoma (10), and squamous cell carcinoma (18). Heat treatments were given with a 500-KHz radiofrequency power source by either capacitive or resistive coupling. Radiation therapy was given by either 4- or 10-MV X-rays, electrons, or orthovoltage. The total tumor dose was 460 rad/fraction given twice weekly for a total of 8 treatments. A comparison of response rates among the three treatment arms showed that the fraction of nonresponders in the heat alone arm (53.3%) was significantly higher than in the other 2 arms combined or the heat plus irradiation arm alone. The relationship between tumor size and response to therapy showed that heat alone and irradiation alone resulted in complete responses

only in tumors less than 35 cm³. In contrast, the combination of the 2 modalities resulted in complete responses in 4 tumors that were larger than 50 cm³. The median response duration for heat alone was less than 2 mo. This was significantly shorter than that for irradiation alone or heat plus irradiation. The major complication was the development of third degree burns from the heat treatments, which occurred in 30% of the subjects in both heat arms. No late complications such as necrosis were observed. This is the first randomized prospective trial to show that heat alone is ineffective for long-term control of most tumors.

0472 BIOLOGICAL RATIONALE FOR OPTIMAL SCHEDULING OF HEAT AND IONIZING RADIATION: CLINICAL RESULTS ON NECK NODE METASTASES. (Eng.) Arcangeli, G. (Istituto Medico e di Ricerca Scientifica, Via S. Stefano Rotondo, 6, 00184 Rome, Italy); Cividalli, A. Creton, G.; Mauro, F.; Nervi, C. *Natl Cancer Inst Monogr* 61:407-409; 1982 (8 refs).

A total of 101 neck node metastases from head and neck cancer were selected from 47 patients and treated with different multimodality schedules. Similar lesions in each patient were treated with at least two modalities. Patients were irradiated according to a multiple daily fractionated (MDF) protocol with 4 hr intervals between fractions; 30/101 nodes were treated with MDF alone. Multimodality treatment combined MDF with the radiosensitizer Misonidazole (MIS: 22 nodes); with hyperthermia (HT) induced by 500 MHz microwave radiation (27 nodes); or with MIS and HT (20 nodes). In the nodes treated by HT, a tumor core temperature of 42-43 C was delivered for 45 min to only one lesion/patient on days 1, 3 and 5 of each wk, immediately after the second daily MDF treatment. Tumor response at the end of 6 and 12 mo was compared. The best results were obtained in cases where HT was combined with MDF or MDF + MIS. In these instances, actuarial local control rates at 12 mo were 73% and 80% of the lesions, respectively. Little toxicity was experienced by patients treated by HT + MDF. No enhanced skin reactions were seen during treatment or follow-up in patients treated with HT, though skill and care are required to avoid burning the patient's skin.

0473 CLINICAL EXPERIENCE WITH MICROWAVE AND RADIOFREQUENCY THERMOTHERAPY IN THE TREATMENT OF ADVANCED CANCER. (Eng.) Abe, M. (Dept. Radiology, Faculty Medicine, Kyoto Univ., 54 Shogoin Kawa-haracho, Sakyo-ku, 606 Kyoto, Japan); Hiraoka, M.; Takahashi, M.; Ono, K.; Nohara, H. *Natl Cancer Inst Monogr* 61:411-414; 1982.

Clinical experience using microwave (MW) and radiofrequency (RF) thermotherapy in the treatment of ad-

vanced cancer is presented. Hyperthermia by 2450-MHz MW radiation in combination with radiotherapy was delivered to 13 patients with superficial neoplasms and metastatic tumors in the neck. Tumors were no more than 2 cm deep and 6 cm in diameter. In 10 patients, hyperthermia to 41-43.5 C was administered for 20-40 min within 10 min after irradiation, 1-5/wk; complete regression (CR) was seen in 3/10 patients, partial regression (PR) in 4, and no response in 3. In 3 patients, MW heat (42.3-43 C for 15 min) was applied before and after irradiation 5/wk; CR was seen in 2/3 patients and no response in 1. To raise the temperatures in middle and deep-seated tumors, an RF device with an output >500 W at an inductor-capacitor oscillator-generated frequency of 13.56 MHz was used to conduct initial clinical trials on 9 patients who had advanced superficial tumors considered not amenable to conventional treatment. Six patients who had developed recurrence after radiotherapy were treated by RF hyperthermia alone (41-46 C for 30-60 min, 4 to 10 treatments) and 3 were given radiation plus RF hyperthermia (41-44 C for 3-40 min, 2 to 10 treatments). Only 1 patient receiving RF hyperthermia alone experienced PR; no response was seen in 5/6. PR was seen in 2/3 patients treated with radiation and hyperthermia, and CR was seen in 1/3.

0474 A PATHOLOGICAL STUDY ON INTRALUMINAL MICROWAVE HYPERTHERMIA IN ESOPHAGEAL CANCER. (Eng.) Qiu, S. L. (Dept. Pathology, Inst. Medical Sciences of Henan, Zhengchow, Henan, People's Republic of China); Li, D. J.; Shao, L. F.; Wang, C. Q. Natl Cancer Inst Monogr 61:415-417; 1982 (3 refs).

Tissue specimens from 21 esophagectomy patients who had been treated with intraluminal microwave hyperthermia alone or in combination with radiation were compared with 20 surgical specimens treated with radiation alone or that had received no treatment before resection. The main manifestations after hyperthermia were necrosis of paracancerous epithelium, small round cell infiltration around the cancerous tissue, and damage of the interstitial vessels. No specific histopathological changes were regarded as hyperthermia-related, but the degree of tumor damage was more severe in the hyperthermia plus radiotherapy group than that of the group receiving irradiation only. While the histopathological changes in the hyperthermia and the control groups were different, no specific reaction has been identified as being a hyperthermia-induced one.

0475 INTRALUMINAL MICROWAVE HYPERTHERMIA IN THE COMBINED TREATMENT OF ESOPHAGEAL CANCER: A PRELIMINARY REPORT OF 103 PATIENTS. (Eng.) Li, D. J. (c/o G. M. Hahn, Div. Radiobiology Research, Dept. Radiology, Stanford Ford Univ. Sch. Medicine, Stanford, CA 94305); Wang, C. Q.; Qiu, S. L.; Shao, L. F. Natl Cancer Inst Monogr 61:419-421; 1982 (5 refs).

Preliminary results of treatment of 103 patients with esophageal cancer using intraluminal microwave hyperthermia and surgery (10 patients) or hyperthermia and radiation (93) are reported. Tumor size was 5 cm or less (36 patients), 5-8.9 cm (74), 9-15 cm (11). Tumors were localized by endoscopy or fluoroscopy. Hyperthermia was induced with a 6-mm diameter microwave antenna with an active length of 105 and 157 mm. The antenna was 3-4 cm longer than the tumor. Treatment temperature was above 43 C. Most patients underwent treatment without discomfort when the esophageal temperature was 43 C; they felt warm but had no pain at 45 C. At surgery, a hyperemic zone on the outer wall of the esophagus and pleura was seen; extensive, small round cell infiltration with stenosis and obliteration of blood vessels in the muscular layer of the resected specimens were indicative of the effectiveness of the hyperthermic treatment.

0476 COMBINATION OF HYPERTHERMIA WITH RADIATION IN THE TREATMENT OF CANCER. I. PRELIMINARY REPORT ON TWENTY-FOUR PATIENTS. (Eng.) Shen, R. N. (Dept. Radiotherapy, Montefiore Hosp. and Medical Center, 111 E. 210 St., Bronx, NY 10467); Wu, H.; Wang, J.; Ku, H. Natl Cancer Inst Monogr 61:423-425; 1982 (3 refs).

Preliminary clinical results in 24 patients with advanced cancer treated with 2450 MHz hyperthermia or radiation therapy (2000-5000 rad) following hyperthermia are reported. In most hyperthermia treatments, tumor temperatures reached 43 C or more. No serious acute complications of hyperthermia were observed. An objective response was seen in 23/24 patients and 23/24 had subjective pain relief. Several complete tumor regressions were seen. The results suggest that hyperthermia enhanced the radiation response.

0477 MODERATE WHOLE-BODY HYPERTHERMIA IN COMBINATION WITH CHEMOTHERAPY IN THE TREATMENT OF SMALL CELL CARCINOMA OF THE LUNG: A PILOT STUDY. (Eng.) Neumann, H. (Medizinisches Universitätsklinik, Hugstetterstrasse 55, D-7800 Freiburg, W. Germany); Fabricius, H-A.; Engelhardt, R. Natl Cancer Inst Monogr 61:427-429; 1982 (19 refs).

Chemotherapy was combined with moderate whole body hyperthermia (WBH) to treat 18 patients with small cell carcinoma of the lung. A Siemens unit, which consists of a Plexiglas cabin preheated with warm air up to 55-60 C, was used to induce WBH. The patient rested on a mattress in which a coil field electrode is connected to a 17-MHz generator. The target temperature (40.5 ± 0.5 C) was reached in 40-50 min; iv injections of Adriamycin and vincristine were given at the selected treatment temperature which was maintained for 1 hr. WBH was administered 1 to 5 times per patient in day

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1 of each 3-wk chemotherapy cycle. Complete remission was seen in 9/18 patients, partial remission in 7, and no response in 1; 1 patient with progressive disease was exposed to WBH only once and was resistant to chemotherapy and radiotherapy. No cardiopulmonary complications, metabolic disturbances, skin burns, neurological lesions, or excessive bone marrow suppression were seen after treatment. There was no evidence of further distribution or stimulation of growth of established metastases during combined treatment. The procedure was well tolerated and appeared to be safe. Preliminary data concerning duration of remission appeared to be encouraging: 8/13 stage C patients treated were in remission at 5 to 28 mo after treatment (most between 7-9 mo) vs. an average of 6-8 mo for patients treated with chemotherapy alone.

0478 TEMPERATURE-CONTROLLED CAVITY SYSTEM FOR MICROWAVE IRRADIATION OF CULTURE CELLS IN VITRO. (Eng.) Vaguine, V. A. (c/o McEuen, Radiation Div., Varian Associates, Palo Alto, CA 94303); Giebel, R. H.; Tanabe, E.; McEuen, A.H.; Hahn, G. M.; Sapareto, S. A.; Li, G. C. Natl Cancer Inst Monogr 61:457-460; 1982 (6 refs).

The effects of 400-1000 MHz electromagnetic fields on cell cultures were investigated under controlled temperature using a cylindrical reentrant radiofrequency (RF) applicator. The RF applicator is in the form of a cylindrical reentrant cavity, which is similar in structure to a shorted section of coaxial cable line, with a narrow gap introduced in the center conductor near one end. The cavity can be tuned to resonance by varying its length; for the frequency range of 400-1000 MHz, the length is nearly a half wavelength (15-35 cm). Microwave power is coupled into the cavity either by the coupling loop in the floor or by a capacitive probe inserted through the sidewall near the top of the cavity. With 60-80 W of input power, the power density in the sample is 135 to 185 W/cm³; peak electric field intensity in the sample is about 150 V/cm. The temperature of the sample holders is regulated by circulating water. The experimental setup for the temperature controlled RF irradiation system includes an RF power signal source with a frequency range of 0.2-3.0 GHz, and a maximum output power of 90 W. The system provides differential cooling for the culture medium, which is contained in the RF applicator cavity. This technique offers several advantages over previously published methods with respect to absorbed power density, accuracy of temperature control and measurement, and efficiency.

0479 MICROWAVE DIRECT-CONTACT APPLICATOR SYSTEM FOR HYPERTHERMIA THERAPY RESEARCH. (Eng.) Vaguine, V. A. (c/o McEuen, Radiation Div., Varian Associates, Palo Alto, CA 94303); Tanabe, E.; Giebel, R. H.; McEuen, A. H.; Hahn, G. M. Natl Cancer Inst Monogr 61:461-464; 1982 (3 refs).

A direct-contact applicator system, designed as a convenient instrument for microwave hyperthermia therapy research at 430 MHz on large laboratory animals, is described. Three dielectric-loaded cylindrical applicator heads provide a range of field sizes from 4 to 48 cm in diameter with the use of removable irises. The polarization of the emitted radiofrequency (RF) field can be varied continuously from linear to circular. Coolant is circulated through a thin chamber on the front surface of the applicator; the surface in contact with the body is a thin flexible membrane that conforms closely to the skin contour. The RF power is generated by an electronically tuned oscillator driving a 200-W solid state amplifier and delivers energy at 430 MHz. Analysis of the heating pattern produced in a static muscle phantom indicated that the maximum temperature occurred about 1.5 cm below the surface, with the 50% maximum temperature point 3 cm below the surface. Maximum measured leakage at a power level of 100 W under the worst possible conditions (with the applicator unterminated) was <0.5 mW/cm² at a distance of 1 m.

0480 HYPERTHERMIA INDUCTION BY 27-MHz FREQUENCY IN CANCER THERAPY. (Eng.) Mendecki, J. (Dept. Radiotherapy, Montefiore Hosp. and Medical Center, Bronx, NY 10467); Friedenthal, E.; Botstein, C.; Sterzer, F.; Paglione, R. Natl Cancer Inst Monogr 61:465-468; 1982 (4 refs).

Experimental and clinical trials to induce hyperthermia in deep-seated tumors with 27-MHz ridged waveguide applicators are described. The open end of the guide is covered with a rubber membrane, and the guide is filled with deionized water which serves to reduce the overall size of the applicator. The inside of the applicator is divided into Plexiglas compartments that permit placing the applicator in a horizontal position without danger of rupturing the membrane. Energy is introduced from a 27-MHz generator with a variable power output (0-500 W). Reflections of 27-MHz power back into the coaxial input port are minimized by the use of two capacitive tuners. The applicator is inserted into a specially constructed treatment table. A saline-filled bag with an adjustable central aperture is placed on the surface of the applicator to circumscribe the area to be heated. Heating patterns were determined in pig muscle with normal blood circulation and in an artificial rectal tumor in a dog. Patients with advanced tumors that included primary carcinoma of the uterus, metastatic carcinoma of the scapula from a primary lung carcinoma, and carcinoma of the prostate underwent RF hyperthermia in conjunction with or following a course of radiotherapy. Varying degrees of pain relief were reported and no serious side effects were noted.

0481 MICROWAVE APPLICATOR FOR HYPERTHERMIC

TREATMENT OF RETINOBLASTOMA. (Eng.) Langendijk, J. J. W. (Dept. Radiotherapy, Univ. Hosp. Utrecht, Catharijnesingel 101, 3500 CG Utrecht, Netherlands). *Natl Cancer Inst Monogr* 61:469-471; 1982 (5 refs).

A special microwave (MW) applicator made of flexible silicone rubber was designed for hyperthermic treatment of retinoblastoma at 2450 MHz. Power is delivered by a low impedance microstripline that encircles the eye at a level just posterior to the lens. Only 20% of the power entering the stripline is absorbed in the eye; 80% leaves the stripline and is absorbed in the load, which generates a nearly uniform power absorption in the eye along the stripline. MW absorption distribution was measured in eye phantoms. A thermal, finite difference computer model of human and rabbit eyes was verified experimentally in rabbit eyes. Satisfactory temperature distributions were obtained (entire retina, 42 C; lens <39 C). The apparatus allows the entire retina and the vitreous body to be heated to therapeutic temperatures without heating the lens above 39 C, which is considerably lower than the cataractogenic temperature. Precise noninvasive measurement of temperatures in the eye is still a problem.

0482 HIGH-FREQUENCY TRANSMITTER FOR THE LOCALIZED HEAT TREATMENT OF THE PROSTATE GLAND. (Eng.) Petrowicz, O. (Inst. Experimental Surgery, Technical Univ. Munich, Ismaningerstrasse 22, D-8000 Munich 80, W. Germany); Scheiblich, J.; Crucius, A.; Erhardt, W.; Wriedt-Lubbe, I.; Ultsch, B.; Blumei, G. *Natl Cancer Inst Monogr* 61:473-476; 1982 (5 refs).

An apparatus consisting of a 433.9 MHz, 200 W generator and a water-cooled 12 mm x 40 mm cylindrical slot antenna for localized heat treatment of the prostate gland was investigated and the morphological changes induced by the irradiation were characterized. The cylindrical cover of the antenna was 20 mm in diameter and the temperature was lowered to 2-10 C by a cooling system so that the maximum heat generated on the applicator surface could be reduced. The prostate glands of 35 mature dogs were irradiated transrectally for 15-20 min by application of 35 to 75 W, resulting in temperatures of 41.5-48 C in the glands. Heat-induced damage of varying degrees to the rectum and surrounding tissues depended on the amount of power applied. Most of these effects could be eliminated by slight modifications of the transmitting and cooling system. It was concluded that power rates of 30-40 W and cooling temperatures of 2-3 C would result in effective local hyperthermia.

0483 MICROWAVE-INDUCED HYPERTERMIA: AN EXPERIMENTAL ADJUNCT FOR BRAIN TUMOR THERAPY. (Eng.) Samaras, G. M. (Neuro-oncology Res. Labs.,

MSTF6-34, Dept. Radiation Therapy and Div. Neurological Surgery, Univ. Maryland Sch. Medicine, 10 S. Pine St., Baltimore, MD 21201); Salzman, M.; Cheung, A. Y.; Abdo, H. S.; Schepp, R. S. *Natl Cancer Inst Monogr* 61:477-482; 1982 (7 refs).

A miniature, implantable microwave (MW) antenna and thermotherapy system was used for interstitial heating in cat and human brain. Adult cats were exposed to 2450 MHz radiation delivered by a surgically-implanted, flexible cable antenna. Heating and cooling in normal feline brain was rapid. Except in places of altered blood flow or tissue necrosis, the heating pattern was nearly radially symmetric. No remarkable physiologic alterations were observed during forebrain heating. While controlling rectal temperature and increasing temperature at the antenna up to +5 C, no significant alterations in blood pressure, intracranial pressure, or EKG were seen. Pupillary size remained unchanged. Histological examination of sham and MW-heated brain showed no significant difference; in both, surgical edema was present probably due to antenna insertion. For the most part, the results of human implantation were similar to those obtained in animals. Monitored arterial blood pressure, intracranial pressure, and EKG were virtually unchanged during the 30 min of heating in the operating suite and subsequent 60-min heating sessions 6 and 48 hr later. Studies of the physical performance and physiological impact of focal MW heating in the forebrain suggest that the implantation method is technically feasible and a relatively simple method for glioblastoma treatment.

0484 SYSTEM FOR PRODUCING LOCALIZED HYPERTERMIA IN TUMORS THROUGH MAGNETIC INDUCTION HEATING OF FERROMAGNETIC IMPLANTS. (Eng.) Stauffer, P. R. (Div. Radiation Oncology, Dept. Radiology, Univ. Arizona Health Sciences Center, Tucson, AZ 85724); Cetas, T. C.; Jones, R. C. *Natl Cancer Inst Monogr* 61:483-487; 1982 (6 refs).

A magnetic induction heating system was developed to heat small ferromagnetic seeds surgically or stereotactically imbedded in deep seated tumors. Induction field frequencies of 1.9 MHz (power, 65 and 300 W), 4.0 MHz (175 W), and 2.0 MHz (200 W) were used to heat static and dynamic tissue equivalent phantoms, feline muscle, and canine muscle *in vivo*, respectively. The uniform temperature distributions seen in cat and dog muscle agreed with results obtained in the phantoms. The data indicated that implant temperature differentials can be maintained within 1.5 x that reached throughout the implanted region, regardless of tissue inhomogeneities. Implant arrays consisting of 1-2 mm stainless steel rods combined excellent heating characteristics in a 1.5-4.0 MHz magnetic induction field with long-term biocompatibility. Power of 200-300 W was sufficient to raise an implantable region of any size to therapeutic temperatures safely in less than 10 min.

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0485 EVALUATION OF AN INVASIVE MICROWAVE ANTENNA SYSTEM FOR HEATING DEEP-SEATED TUMORS. (Eng.) Strohbehn, J. W. (Thayer Sch. Engineering, Dartmouth Coll., Hanover, NH 03755); Tremblay, B. S.; Douple, E. B.; de Sieyes, D. C. Natl Cancer Inst Monogr 61:489-491; 1982 (6 refs).

A mathematical model was developed to predict temperature distributions for a multiple antenna system in which numerous small microwave (MW) antennas are inserted into tissue or tissue phantom through hypodermic needles. A single MW source attached to a power splitter usually feeds all the antennas simultaneously. A heat equation based on a two-dimensional model that ignores heat flow along the axial direction of the antennas was solved by the Alternating Direction Method. Blood flow and metabolic effects were not included in the model. Isotemperature contours were calculated and plotted for a frequency of 1.0 GHz, and antenna circles with a radius of 1.414, 2.12, and 2.828 cm, and 3-5, 4-6, and 4-8 antennas, respectively. For an antenna circle with a radius of 1.414 cm and 4 antennas, temperature reached therapeutic levels (+2-+5 °C) within 15 min; the diameter of the heating volume was 3 cm. Five and eight antennas, respectively, were required to produce 4 and 7 cm heating volumes within 15 min.

0486 DEEP HEATING OF CYLINDRICAL OR ELLIPTICAL TISSUE MASSES. (Eng.) Turner, P. F. (BSD Medical Corp., 420 Chipeta Way, Salt Lake City, UT 84108). Natl Cancer Inst Monogr 61:493-495; 1982 (3 refs).

A new technique for producing uniform heating to the center of large tissue masses, i.e., thorax and abdomen, is described. The prototype BSD applicator is an annular phased array composed of radiating apertures operated in the transverse electromagnetic (EM) mode. The patient lies inside a central opening; a water-filled bolus or bladder placed between aperture walls and patient improves energy coupling, stray-field level, and surface-temperature control. The radiation field of the array is a cylindrically convergent transverse EM wave with the electrical field polarized along the cylindrical axis. Measured cylindrical cross-section heating patterns in a homogeneous muscle-equivalent phantom are shown. Temperature rise during rapid heating was monitored at 31 positions within the phantom. Some nonsymmetry was observed attributed in part to the phantom's elliptical shape. Heating experiments with the annular phased array were conducted on a 240-pound pig with chest and pelvic dimensions similar to those of an adult man. A therapeutic temperature of 42.5 °C was maintained for 30 min 3-4 cm deep in chest and abdominal regions. No resulting ill effects were observed in the animal for 6 days following the treatment. The animal was then killed to study heating patterns in the absence of blood circulation. The thoracic heating pattern (794 W for 9.8 min) showed heating in

the esophageal region to be twice that of tissues outside the rib cage. In the central lung area, the heating rate was 1.2 times that of the outer tissues. Rapid heating (2,000 W for 10.7 min) of the pelvis resulted in a uniform pattern. The lowest central temperature rise was 70% of the maximum at 3 cm depth. It is concluded that therapeutic heating can be achieved even in deep tumor sites.

0487 HYPERTHERMIA INDUCTION BY AN ARRAY OF INVASIVE MICROWAVE ANTENNAS. (Eng.) Tremblay, B. S. (Thayer Sch. Engineering, Dartmouth Coll., Hanover, NH 03755); Strohbehn, J. W.; de Sieyes, D. C.; Douple, E. B. Natl Cancer Inst Monogr 61:497-500; 1982 (3 refs).

Temperature distributions produced by an array of four insulated antennas radiating at 2 GHz were measured in brain phantom, human brain at autopsy, and muscle tissue of a living dog. A 3-cm (side length) array was used for the cadaver and dog tissue, and 2-, 3-, and 4-cm arrays were used in the phantom. The time required for the temperature to reach therapeutic range increased rapidly with increase in array size; thus square arrays (i.e., 4 antenna arrays) of greater than 3 cm/side may not be clinically useful. Although heating a cadaver brain was similar to heating brain phantom, blood flow in living tissue greatly increased the power required to produce therapeutic temperatures. Steady-state power levels needed to maintain a 6.5 °C antenna temperature were 7.5 W for phantom, 10 W for cadaver, and 20 W for living dog muscle.

0488 DOSIMETRY OF INTERSTITIAL THERMORADIOThERAPY. (Eng.) Cetas, T. C. (Div. Radiation Oncology, Dept. Radiology, Univ. Arizona Health Sciences Center, Tucson, AZ 85724); Hevezi, J. M.; Manning, M. R.; Ozimek, E. J. Natl Cancer Inst Monogr 61:505-507; 1982 (5 refs).

The dosimetry involved in one method of producing combined interstitial heat and radiation treatments for accessible tumors is described. The technique employs a modified electrosurgery unit (500 kHz) with an appropriate matching network as a power source and conventional catheter-mounted thermistors with a digital multimeter for thermometry. An array of 17-gauge hollow needles is inserted through a Plexiglas template into the tissues (up to 15 cm deep) so that the tumor volume is encompassed. The array, determined by the template, can be either of circular or rectangular symmetry. Thermistors also are inserted through the template. Radiofrequency power is applied to heat resistively the tissue between the needle electrodes. A typical treatment is 44 °C for 30 min. Following the heat treatment, the needles are after-loaded with ¹⁹²Ir seeds. The thermal dose is determined from temperature measurements and compared

with analytical and phantom models which use measured thermal and electrical parameters. Computed radiation isodose curves are based on actual seed locations determined from the needle arrangement and from orthogonal projection radiographs. It is concluded that interstitial thermoradiotherapy is safe and effective for treating patients with advanced local disease.

0489 THERMAL DOSIMETRY DURING HYPERTERMIA.
(Eng.) Ozimek, E. J. (General Products Div., IBM Corp., 74B/061-2, Tucson, AZ 85744); Cetas, T. C. Natl Cancer Inst Monogr 61:509-512; 1982 (6 refs).

Maximum therapeutic benefit from hyperthermia in cancer treatment requires knowledge of temperature profiles throughout the heated tissue volume. The bioheat equation relates internal energy change rates to heat generation and dissipation processes. Energy deposition and subsequent temperature distribution can be predicted if electrical conductivity and permittivity and effective thermal conductivity are known. The *in vivo* thermal properties of various normal tissues in laboratory minipigs as well as in humans were measured. Temperatures were measured with calibrated thermistor probes at several points in tissues heated with microwave and with water bath techniques, and the results were incorporated in a numerical solution of the bioheat equation. Temperature profiles determined for minipig thighs heated at 2,450 and 915 MHz showed good agreement between measured and predicted temperatures; blood flow was the only adjustable parameter. At 2,450 MHz, the tissue blood perfusion rate yielding the best temperature depth profile agreement was 0.0010 g of blood/cm³ of tissue/sec.

0490 THERMAL DOSIMETRY SYSTEM WITH BLOOD FLOW SIMULATION. (Eng.) Sandhu, T. S. (Div. Radiation Oncology, Univ. Utah Coll. Medicine, Salt Lake City, UT 84132). Natl Cancer Inst Monogr 61: 513-515; 1982 (7 refs).

A dynamic phantom system was developed for studying temperature distributions produced by external heat sources in tissue-equivalent materials under different blood flow conditions. The system is designed for use with noninvasive heat transducers, such as direct-contact, microwave waveguide applicators or ultrasound transducers. The dynamic phantom consists of a Plexiglas chamber divided into three compartments: the top compartment is filled with liquid maintained at 37°C to simulate *in vivo* conditions; the second contains foam through which the liquid flows; and the third is a thermal insulator. Thermocouples measure temperature at different points in the foam. Flow is simulated in one direction (along

the positive x-axis), but temperature distribution in the presence of counter flow can be obtained by data manipulation. Measurements at three flow rates (0, 200, and 300 ml/min) were made for a 915-MHz applicator (35 W for 5 min). The zero flow curve showed a slight asymmetry due to heat conduction to the chamber's lower portion, whereas the liquid temperature was kept at 37°C. At significant flow rates, peak temperature position was depressed (positive x direction), and temperatures beyond the applicator dimensions were significantly greater than 37°C. Under counter flow conditions, temperature distributions were significantly altered near edges of the applicator field. At depths of 1 cm or greater from the applicator face, there was a decrease in temperature but no change in the pattern. Limitations of the system are summarized.

0491 PULSED MICROWAVE THERMOMETRY: AN ALGORITHM FOR THERMAL PERTURBATION. (Eng.) Loshek, D. D. (Section Medical Physics, Marshfield Clinic, Marshfield, WI 54499). Natl Cancer Inst Monogr 61: 517-520; 1982 (no refs).

A pulsed microwave (MW) diathermy system that uses ordinary thermistor temperature sensors is presented. Temperature signals from the thermistor sensors are sampled under computer control during the "off" state of the pulsed MW generator. These temperature signals are compared with the desired temperature, and the duty cycle of the microwave generator is adjusted to yield regulation about the preset temperature. Because blood perfusion produces rapid cooling of locally heated tissue, the computer has been programmed to produce a MW pulse lasting from 0 to 500 msec once each second. A residual perturbation of the temperature signal often interferes with the measurement during this short period. The nature of this residual perturbation was investigated by analysis of the temperature signal from a thermistor probe placed in a piece of plastic tubing through which water at a constant temperature was flowing. Alterations of the temperature signal could in this manner be attributed solely to the microwave perturbation of the sensor and not to MW heating of the environment. Perturbation magnitude increased with length and energy of the pulses. The perturbation decayed exponentially with a time constant that was independent of pulse length but that increased with water flow rate through the tubing. The computer algorithm presented herein in conjunction with sufficiently fast thermistor probes may enable pulsed temperature measurements with a wider variety of microwave equipment and clinical situations.

0492 COMPUTER SOLUTION FOR APPLICATOR HEATING PATTERNS. (Eng.) Turner, P. F. (BSD Medical Corp., 420 Chipeta Way, Salt Lake City, UT 84108); Kumar, L. Natl Cancer Inst Monogr 61:521-

523; 1982 (4 refs).

A mathematical solution is presented to the problem of predicting heating patterns in tissue located in a microwave applicator's near-field region. The solution was used to obtain information regarding the effects of frequency, applicator size, aperture field distribution, and low-loss bolus materials on penetration depth and heating patterns. The model solution was extended to both flat surface and cylindrical apertures and to a new array applicator. Heating patterns were predicted for each at many different frequencies. A significant finding was the limited penetration depth of radiative applicators. By correcting for non-homogeneous losses, reflection, and refraction, accurate power absorption rate predictions can be obtained for living systems. When coupled with the blood heat-flow dynamics of the body, temperature rise can be predicted.

0493 RAPPORTEUR SESSION: HEATING TECHNIQUES.
(Eng.) Durney, C. H. (Depts. Electrical Engineering and Bioengineering, Univ. Utah, Salt Lake City, UT 84112). Natl Cancer Inst Monogr 61:525-528; 1982 (no refs.).

Basic problems and the state of the art in hyperthermia production and measurement techniques and the contributions presented at the Third International Symposium: Cancer Therapy by Hyperthermia, Drugs, and Radiation held at Colorado State University, Ft. Collins, Co, June 22-26, 1980 (National Cancer Institute Monograph 61) are summarized. The material presented is based on a summary presented by the author in a session devoted to discussion of the poster papers on heating techniques and on the resulting discussion by the audience.

0494 THE FUTURE OF HYPERTHERMIA. (Eng.) Tubiana, M. (Dept. Radiation, Institut Gustave-Roussy, 16 bis avenue Paul-Vaillant Couturier, 94800 Villejuif, France). Natl Cancer Inst Monogr 61:539-543; 1982 (19 refs.).

Differences in response to heat of human tumors are a major obstacle to thermotherapy progress. Xenografts of human tumor in nude mice or preferably in nude rats may provide an effective tool for the study of those biological factors which may influence the effect of heat on a tumor or a normal tissue. Probably, physical factors are the most important sources of difference. The development of a unit dose embodying the amount of heat transferred to the tissues as well as quality factors is a goal for the future. However, the relationships between heating time and temperature required to produce various biological effects are open to discussion, and presently there is no

substitute to the recording of both temperature and time. The search for optimal scheduling requires knowledge of dose-effect relationships for both normal tissue tolerance and tumor regression. The development of small size probes and of noninvasive thermodosimetry is a prerequisite for widespread clinical use of hyperthermia. Heat alone constitutes an important modality of hyperthermia but its use as routine palliative therapy is still unwarranted. Treatments should be aimed at the identification of those tumor types which are responsive to hyperthermia, and they must be considered as clinical investigations conducted within controlled clinical trials. Attention should be given to the reporting of heating techniques. The rate of heating must be precisely stated. For each patient, the spatial and temporal temperature distributions must be given as well as the method used for temperature monitoring. Each tumor should be described precisely and the treatment effects assessed quantitatively both on tumor and normal tissues. Immediate as well as late side effects should be recorded. Treatment by heat alone also provides a good opportunity for assessment of the effects of manipulation of pH or of blood flow. Enhancement by heat of radiation effects is critically dependent on the time and sequencing. For an interval between heat and radiation of 1 hr or a few hours, potentiation is obtained. At 24 hr, the biological effects of the two modalities are independent and purely additive. The combination of heat and irradiation has been used mainly for palliative treatment of large inoperable tumors or for metastases. As soon as an adequate temperature monitoring system is available, controlled trials on potentially curable tumors can begin. Hyperthermia shows synergism with many drugs for both normal and neoplastic cells. Because heat has no harmful effects on bone marrow, it could be delivered between chemotherapy cycles when leukopenia and thrombopenia prevent extended radiotherapy. Even when chemotherapy is combined with local radiotherapy, hyperthermia might allow reduction of the radiation field and/or dose.

0495 CHANGES IN BLOOD COAGULATION AFTER LUNG SURGERY AND EXPOSURE TO A CONSTANT MAGNETIC FIELD. (Rus.) Novikov, Iu. A. (Dept. Hosp. Surgery, Medical Inst., Ivanovo, USSR). Anesteziol Reanimatol (3):21-23; 1982 (4 refs.).

Potentially favorable effects of postoperative exposure to a constant magnetic field (CMF) were studied in 184 patients (146 men, 38 women; 30-60 yr old) subjected to lobectomy or pneumonectomy. The patients were divided into two groups: Group 1 (130 patients) received conventional postoperative analgesia with narcotic substances, while Group 2 (54) received applications of 2-3 magnetic plates at the site of the surgical incision and on the thoracic region of the spinal column. CMF produced pain relief in 41% of the patients. Tests of blood coagulation showed marked inhibition of fibrinolysis with simultaneous activation of blood coagulation in Group 1. The pati-

ents in Group 2 showed normalization of the heparin level, fibrinolytic activity, and time of thromboplastin formation. Improvement of blood coagulation indices was not correlated with the analgesic effect of CMF. It was concluded that the negative charge acquired by the blood-formed elements after exposure to CMF maintains them in a suspended state and prevents sequestration and sludging.

496 MORPHOLOGICAL CHARACTERISTICS AND THE MECHANISM OF BIOLOGICAL EFFECTS OF MAGNETIC FIELDS. (Rus.) Toroptsev, I. V. (Dept. Pathology, Medical Inst., Tomsk, USSR); Taranov, S. V. *Arkhiv Patologii* 44(12):3-12; 1982 (96 refs).

Literature data on the mechanism of biological effects of magnetic fields are reviewed. Numerous studies confirmed the greater biological activity of alternating and pulsed magnetic fields compared with constant magnetic fields. Biological parameters of magnetic fields include the intensity, gradient, direction of the vector, duration of exposure, and frequency. Even short-term exposure to magnetic fields was shown to produce marked morphological changes in the nervous and endocrine systems. Morphological changes in the cardiovascular system after exposure to magnetic fields were characterized by circulation disorders, increase in capillary permeability, development of interstitial edema, dystrophy, and necrosis of vascular walls. Exposure to weak and moderate magnetic fields (intensity of 20 to 7,000 Oe) produced swelling of Kupffer cells, increase in the proliferative pool and mitotic activity of enterocytes in the small intestine, and increase in the metabolic activity of liver and small intestine cells. The mechanism of biological action of magnetic fields is associated with primary interactions between the magnetic field and the biological substance, reception by the biological object of the magnetic field, and response of the biological object to the magnetic field.

497 MAGNETIC SUSCEPTIBILITY OF SINGLE HUMAN ERYTHROCYTES. (Rus.) Kondorskii, E. I. (Physics Dept., M. V. Lomonosov State Univ., Moscow, USSR); Norina, S. B.; Litvinchuk, N. V.; Shalygin, A. N. *Biofizika* 26(6):1104-1106; 1981 (8 refs).

A method of measuring the magnetic susceptibility of isolated human erythrocytes is described. The movement of erythrocytes in a heterogeneous magnetic field of thin ferromagnetic wire ($8 \times 10^{19} \text{ A}^2/\text{m}^3$) was monitored by a specially designed movie camera. Analysis of the distribution of erythrocytes and the relationship between the magnetic susceptibility and the velocity of erythrocytes showed that the magnetic susceptibilities of erythrocytes containing methemoglobin, deoxyhemoglobin, and oxyhemoglobin were $(0.54 \pm 0.05)/10^6$, $0.46 \pm 0.05/10^6$, and $(-0.75 \pm 0.05)/10^6$,

respectively.

0498 MAGNETIC SUSCEPTIBILITY OF RHODOPSIN. (Rus.) Vilenchik, M. M. (Inst. Biological Physics of USSR Acad. Sciences, Pushchino, Moscow Region, USSR). *Biofizika* 27(1):31-36; 1982 (31 refs).

To test the hypothesis that the physical mechanism of biological effects of a constant magnetic field is associated with the anisotropy of magnetic susceptibility of protein molecules, the anisotropy of rhodopsin molecules in photoreceptor membranes was calculated. Assuming that the anisotropy of rhodopsin is determined by orientation of aromatic amino acids and peptide bonds, it was calculated that the majority of the external segments of the retina were oriented along the force lines of the magnetic field with an intensity of approx. 80 Oes ($6.4 \times 10^3 \text{ A/m}$). Duration of the orientation of the external segment of the frog cone was approximately 10 sec for a field of intensity of $8 \times 10^5 \text{ A/m}$ and approximately 24 hr for fields of threshold intensity ($6.4 \times 10^3 \text{ A/m}$). Potential applications of the observed orientation of protein molecules in constant magnetic fields include cancer chemotherapy (administration of liposomes containing an antineoplastic agent and ferromagnetic filler) as well as inhibition of tumor growth in the magnetic anisotropy of membrane proteins from normal and tumor cells.

0499 EFFECT OF HIGH-FREQUENCY ELECTROMAGNETIC FIELDS ON TETRA-PHENYL-BORATE TRANSPORT THROUGH BILAYER LIPID MEMBRANES. (Rus.) Alekseev, S. I. (Inst. Biological Physics, USSR Acad. Sciences, Pushchino, Moscow Region, USSR); Tiazhelov, V. V.; Faizova, L. Kh.; Chertishchev, V. V. *Biofizika* 27(1):162-163; 1982 (8 refs).

The effects of high-frequency electromagnetic fields (0.9 GHz) on the transport of tetraphenylborate (TPB) ions through the bilayer lecithin membrane were studied in sodium chloride solution. TPB transport was established by changes in the saturation current. The increase in the membrane saturation current was proportional to the electrolyte concentration and to the specific absorbed power (up to 200 W/kg), and did not depend upon TPB concentration (within a 10^{-4} - 10^{-5} M range). The increase in the electrolyte temperature by 10°C resulted in a 1.8-fold increase in the saturation current. These findings indicated that the effects of high-frequency electromagnetic fields were associated with local heating of the electrolyte layer adjacent to the membrane.

0500 THE ABSENCE OF EFFECT OF MAGNETIC FIELDS ON SODIUM, POTASSIUM ION-DEPENDENT ATPASE.

Current Literature

Biological Effects of Nonionizing Electromagnetic Radiation VII(2-4), July 1983

(Rus.) Savich, M. L. (Res. Inst. Biological Testing of Chemical Compounds, Kupavna, Moscow Region, USSR); Shcheglova, M. V.; Raikhman, L. M.; Kuznetsov, A. N. Biofizika 27(3):532-533; 1982 (3 refs).

To evaluate the direct effects of magnetic fields on sodium, potassium ion-dependent ATPase, the membrane preparation of enzyme isolated from bovine brain was exposed to an electromagnetic field (EMF) with inductance of up to 1,500 mT. The experiments were conducted at 15 C, 20 C, and 37 C. Sodium, potassium ion-dependent ATPase activity was estimated by the amount of released inorganic phosphate. Duration of exposure was 15 min. Exposure to EMF did not affect enzyme activity, Michaelis constant for ATP, activation constants for sodium and potassium ions, or Hill coefficients for ATP and ions. It was concluded that EMF with inductance of up to 1,500 mT had no direct effect on isolated enzyme preparations, and that the changes in active transport after exposure to EMF were associated with the effect on regulators of sodium, potassium ion-dependent ATPase.

0501 MECHANISM OF MICROWAVE EFFECT ON CONDUCTANCE OF BILAYER LIPID MEMBRANES. (Rus.) Alekseev, S. I. (Inst. Biological Physics, USSR Acad. Sciences, Pushchino, Moscow Region, USSR); Chertishchev, V. V.; Kim, Iu. A. Biofizika 27(3):545-546; 1982 (7 refs).

The effects of microwave radiation (MW) on the conductance of modified bilayer lipid membranes (BLM) were studied. Changes in the conductance of BLM modified with amphotericin B, gramicidin C and tetraphenylborate showed a linear relationship with the specific absorption rate (SAR) and was proportional to the changes in the temperature. Temperatures of the BLM equivalent to the changes in the conductance after exposure to a SAR of 200 W/kg were 7.2 C for BLM membranes modified with amphotericin B, 6.3 C for gramicidin C-modified BLM, and 6.2 C for tetraphenylborate-modified BLM. It was concluded that the mechanism of MW effects was associated with local heating of BLM.

0502 NONTHERMAL EFFECT OF EXTREMELY HIGH FREQUENCY PULSES OF NANOSECOND DURATION ON TRANSEPITHELIAL TRANSPORT OF SODIUM IONS. (Rus.) Deviatkov, N. D. (Inst. Radio Engineering and Electronics of USSR Acad. Sciences, Moscow, USSR); Chernov, Z. S.; Betskii, O. V.; Novskova, T. A.; Putinskii, A. V. Biofizika 27(3):552-554; 1982 (5 refs).

Nonthermal effects of pulsed microwave (MW) radiation on the transepithelial transport of sodium ions were studied in isolated frog skin. The MW source was a NS generator (10 nanosec pulses, peak power 30 mW, and

3 cm wavelength). Exposure of skin specimens to MW pulses resulted in reversible activation of sodium transport. The increase in the transepithelial sodium transport could be associated with the increase in sodium, potassium-dependent ATPase as well as the increase in membrane permeability.

0503 HYDROLYSIS OF GLOBULAR PROTEINS WITH TRYPSIN IN A STRONG MAGNETIC FIELD. (Rus.) Nazarova, N. M. (Res. Inst. Biological Testing of Chemical Compounds, Kupavna, Moscow Region, USSR); Livshits, V. A.; Anzin, V. B.; Veselago, V. G.; Kuznetsov, A. N. Biofizika 27(4):720-721; 1982 (8 refs).

To evaluate possible physico-chemical mechanisms of biological effects of magnetic fields, hydrolysis of various globular proteins with trypsin was studied in a strong (up to 10 T) magnetic field. Incubation of trypsin with serum albumin or with methemoglobin resulted in an approximately 48% yield of the hydrolysis products. Kinetics of hydrolysis after exposure to a magnetic field with inductance of 1.4 or 10 T did not differ from that in control. The magnetic field also did not affect the rate of proteolysis with the use of immobilized trypsin. These findings indicated that strong magnetic fields had no effect on the kinetics of hydrolysis of globular proteins.

0504 THE ABSENCE OF EFFECT OF A MAGNETIC FIELD ON OXYGEN SOLUBILITY IN AQUEOUS SOLUTIONS. (Rus.) Ushakova, T. V. (Res. Inst. Biological Testing of Chemical Compounds, Kupavna, Moscow R., USSR); Livshits, V. A.; Kuznetsov, A. N. Biot. 27(5):757-761; 1982 (10 refs).

To evaluate whether the potential mechanism of biological activity of magnetic fields (MF) is associated with changes in solubility or molecular mobility of paramagnetic oxygen the rate of oxygen solubility in distilled water or in an aqueous solution of sodium chloride was studied. Exposure of solutions to permanent MF with inductance of 0.35 T did not change oxygen solubility in distilled water or in the electrolyte solution. The absence of an effect on oxygen solubility was observed for both homogeneous and heterogeneous MF with gradient of 10 T²/m. These findings indicated that the MF of an order of 0.1 T did not alter the rate of solubility and the coefficients of oxygen diffusion.

0505 SCAR BASALGMA FOLLOWING MICROWAVE THERAPY. (Ger.) Ippen, H. (Universitäts-Hautklinik, 3400 Gottingen, W. Germany). Berum Beruf Umwelt 30 (2):60; 1982 (2 refs).

A 57-yr-old woman presented with a basal cell carcinoma which had developed in a burn scar on her back. The burn resulted from exposure of the metal hooks on her brassiere to microwave radiation during treatment 6 yr earlier. The patient was not aware that the burn had occurred until the following morning when she experienced slight discomfort. This case serves as a reminder that skin burns can be caused by therapeutic use of 10-300 MHz and 2450 MHz radiation if the skin comes into contact with metal during treatment.

0506 MAJOR RESEARCH ON THE BIOLOGICAL EFFECTS OF MICROWAVE RADIATION IN THE USSR (Rus.) Shandala, M. G. (Kiev, USSR); Rudnev, M. I.; Stoian, E. F.; Vinogradov, G. I. *Gig Sanit* (10): 4-7; 1981 (20 refs).

Studies of the biological effects of low intensity (1-1,000 $\mu\text{W}/\text{cm}^2$) microwave (MW) radiation conducted in the USSR are reviewed. Characteristic features of the Soviet investigations include prolonged (up to several mo), daily exposure (from several hr/day to 24 hr/day) of different animals with follow-up examinations for 1-3 mo after completion of the irradiation. Analysis of adaption reactions after exposure to MW indicate that power flux densities of 500 and 50 $\mu\text{W}/\text{cm}^2$ caused certain changes in the central nervous system and in the immune system, while MW at 10 $\mu\text{W}/\text{cm}^2$ stimulated adaptation reactions (subthreshold levels) and MW at 1 and 5 $\mu\text{W}/\text{cm}^2$ failed to induce any functional changes. Examinations of humans with occupational exposure to MW revealed functional and neurological changes. The incidence and severity of the observed changes depended upon the duration of exposure, the wavelength, and the type of electromagnetic field (pulsed or continuous).

0507 FUNCTION OF THE HYPOPHYSAL-ADRENAL SYSTEM AFTER EXPOSURE TO DIFFERENT REGIMENS OF ALTERNATING MAGNETIC FIELDS OF INDUSTRIAL FREQUENCY. (Rus.) Udintsev, N. A. (Medical Inst., Tomsk, USSR); Moroz, V. V. *Gig Tr Prof Zabol* (12):54-56; 1982 (16 refs).

To determine the maximum permissible levels of exposure to alternating magnetic fields (AMF: 20 mT) of industrial frequency (50 Hz), albino male rats were subjected to either continuous AMF exposure (for a period of several sec to 7 days) or to interrupted AMF exposure (15 min/day or 6.5 hr/day for 7 days, or 15 min with 2-hr intervals between exposures). The effects of AMF were estimated by the functional activity of the hypophyseal-adrenal system. Continuous exposure to AMF resulted in increased blood levels of 11-hydroxyketosteroids, an increase in the levels of adrenocorticotrophic hormone (ACTH) in the pituitary gland and in the blood, and in an increase of steroid levels in the myocardium. The effects of AMF during

interrupted exposure depended upon the periodicity and duration of exposure. Prolonged repeated exposures (6.5 hr/day for 7 days) produced marked inhibition of the corticotrophic function of the pituitary gland and of steroid hormone synthesis in the adrenal glands.

0508 ELECTRIC POWER TRANSMISSION LINES AS A SOURCE OF ELECTROMAGNETIC FIELDS AND THE PROBLEM OF ENVIRONMENTAL HYGIENE. (Rus.) Dumanskii, Iu, D. (Res. Inst. General & Community Hygiene, Kiev, USSR); Andrienko, L. G.; Gordynia, N. P.; Liubchenko, S. A. *Hygiene of Residential Areas* (20):18-22; 1981 (no refs).

To evaluate the health hazards associated with electric power transmission lines, the biological effects of an industrial frequency (50 Hz) electric field were studied in albino rats and human volunteers. Chronic exposure of animals to electric fields with intensities of 5000, 2000, 500, and 100 V/m produced marked changes in animal behavior, hyperemia of eye and nasal mucosa, decrease in blood cholinesterase activity and SH-group content, increase in urinary excretion of 17-ketosteroids, inhibition of oxidative phosphorylation, and changes in brain, myocardium, liver, kidney, and thyroid tissues. The minimum effective intensity after exposure for 24 hr/day for 4 mo was 1000 V/m. The minimum effective intensity after 2 hr/day exposure for 4 mo was 7000 V/m. Examination of human volunteers exposed to an electric field 2 hr/day for 1 mo demonstrated the safety of an intensity of 5000 V/m. It was recommended that the maximum permissible exposure levels should be established at the level of 0.5 kV/m for 24 hr/day exposure, 5 kV/m for short-term exposure (< 2 hr/day), and 15 kV/m for sporadic exposure.

0509 EFFECT OF 50-Hz ELECTROMAGNETIC FIELD ON FORMATION OF COMPLEX CONDITIONED REFLEXES IN ALBINO RATS. (Rus.) Bezsol'naia, I. S. (Res. Inst. General & Community Hygiene, Kiev, USSR). *Hygiene of Residential Areas* (20):22-25; 1981 (7 refs).

Potential biological effects of electromagnetic fields (EMF) of industrial frequency (50 Hz) were investigated in albino rats. The animals were subjected to daily, 6-hr exposure to EMF of 20, 15, and 10 kV/m intensity for 4 mo. The effects of the EMF were estimated by the latent period of food-motor reflex and escape reaction. Exposure to 50-Hz EMF affected the interaction of stimulation and inhibition processes in the cerebral cortex. The changes in the latent period of conditioned reflexes depended upon the intensity of EMF and the duration of exposure. During the first mo of exposure, all animals showed elongation of the latent periods, while during the third mo of

exposure, only the rats exposed to 10 and 15 kV/m EMF showed significant decrease in the latent period.

0510 EFFECTS OF AN EXTREMELY HIGH FREQUENCY ELECTROMAGNETIC FIELD (2,375 MHz) ON VARIOUS FUNCTIONAL AND MORPHOLOGICAL PARAMETERS IN ONTOGENESIS. (Rus.) Shandala, M. G. (Res. Inst. General and Community Hygiene, Kiev, USSR); Rudnev, M. I.; Obukhan, E. I.; Akimenko, V. Ia.; Chernen'kii, N. N. Hygiene of Residential Areas (20):26-29; 1981 (5 refs).

Age-related characteristics of sensitivity to extremely-high frequency (EHF) electromagnetic fields (EMF) were studied in young, mature, and old albino rats. The EHF EMF was generated by a Luch-58-1 apparatus (2,375 MHz, 50mW/cm²). The animals were irradiated with the E-component of the EHF EMF. Exposure to EHF EMF produced marked physiological changes indicative of the stimulation or inhibition of the central nervous system. Old rats showed a marked increase in the threshold of galvanic skin response. Old rats also showed the greatest increase of rectal temperature (by 4.1 C, compared with 2.1 C and 3.9 C in young and mature rats, respectively). The effects of EHF EMF on the bone marrow included increase in lymphocyte count, release of neutrophils, and subsequent hyoplasia of immature precursors of granulocytopenia. The hematopoietic changes in mature and old rats were more pronounced than those in young animals.

0511 IMMUNOLOGICAL AND HEMATOLOGICAL EFFECTS OF LOW-INTENSITY EXTREMELY-HIGH FREQUENCY ELECTROMAGNETIC FIELDS. (Rus.) Vinogradov, G. I. (Res. Inst. General and Community Hygiene, Kiev, USSR); Gonchar, N. M.; Belonozhko, N. G.; Zhelezniak, A. A.; Vinarskaia, E. I. Hygiene of Residential Areas (20):29-33; 1981 (3 refs).

The effects of low-intensity microwave (MW) radiation on various immunological and hematological indices were studied in guinea pigs and in random-bred albino rats. The animals were subjected to daily MW irradiation (2,375 MHz, wavelength of 12.6 cm, power flux density of 500, 50, 10, 5, and 1 uW/cm²; 7 hr/day, for 30 days). MW at 500 uW/cm² and 50 uW/cm² caused inhibition of the phagocytic function of the neutrophils, while MW at a lower power flux density produced stimulation of phagocytosis. MW at 500 and 50 uW/cm² caused marked inhibition of cellular immunity estimated by phytohemagglutinin-induced reaction of T-lymphocytes blast-transformation. MW at 50 uW/cm² induced formation of autoantibodies against the brain and liver. Cytochemical studies showed significant increase in glycogen content and alkaline phosphatase activity in the peripheral blood neutrophils of the animals exposed to MW at 10 and 50 uW/cm². MW at 500

uW/cm² resulted in a transient inhibition of neutrophil cytochemical activity.

0512 HYGIENIC EVALUATION OF A 20-22 kHz ELECTROMAGNETIC FIELD (ELECTRICAL COMPONENT). (Rus.) Kochergin, S. M. (Res. Inst. General and Community Hygiene, Kiev, USSR). Hygiene of Residential Areas (20):33-36; 1981 (no refs).

To evaluate potential health hazards of 20-22 kHz electromagnetic radiation emitted by an Elektronika induction furnace (maximal intensity of 60 V/m was recorded at a distance of 0.1-0.15 m from the edge of the furnace), random-bred albino rats were exposed to an electric field of 5, 1, and 0.5 kV/m. The electric field was generated by a parallel-plate capacitor. The animals were subjected to three exposures of 180 and 45 min each. Exposure to the electric field at intensities of 5 and 1 kV/m caused progressive inhibition of cerebral cortex activity (increased latent period of conditioned reflexes, decreased response to a positive stimuli), decrease in responses to electric stimulation, decrease in muscular endurance, decrease in blood urea and nitrogen concentrations, decrease in cytochrome oxidase activity, increase in blood glucose level, decrease in liver glycogen levels, and increase in ascorbic acid levels. An electric field with an intensity of 0.5 kV/m failed to induce changes in the physiological and biochemical parameters tested. These findings indicated that the intensity of 0.5 kV/m can be accepted as a maximum permissible exposure level.

0513 CONDITIONED REFLEXES IN ANIMALS EXPOSED TO LOW INTENSITY PULSED EXTREMELY HIGH FREQUENCY ELECTROMAGNETIC FIELDS. (Rus.) Zotov, S. V. (Res. Inst. General and Community Hygiene, Kiev, USSR). Hygiene of Residential Areas (20):36-39; 1981 (3 refs).

To evaluate the health hazards of modern radiolocation systems, albino rats were subjected to continuous exposure to pulsed electromagnetic fields (EMF) with a 3-cm wavelength and intensities of 40, 25, and 10 uW/cm². The biological effects of EMF were estimated by the changes in formation of the conditioned food reflex. Exposure to EMF at 40 uW/cm² resulted in progressive increase in the latent period of conditioned reflex. EMF with intensities of 25 and 10 uW/cm² failed to induce significant changes in the formation of food reflexes. These findings indicated that low-intensity EMF can have an unfavorable effect on the central nervous system.

0514 COMPARATIVE CHARACTERISTICS OF THE BIOLOGI-

CAL EFFECTS OF 3-cm AND 8-mm ELECTROMAGNETIC FIELDS. (Rus.) Los', I. P. (Res. Inst. General and Community Hygiene, Kiev, USSR); Tomashevskaya, L. A.; Nikitina, N. G. *Hygiene of Residential Areas* (20):39-44; 1981 (3 refs).

The results of factor analysis of biological effects of 3-cm and 8-mm electromagnetic fields (EMF: pulse duration of 1.2 usec, sample frequency of 800 Hz, bell-shaped pulses) are reported. Random-bred rats were irradiated 12 hr/day for 4 mo; the power flux densities were 5, 60 and 115 $\mu\text{W}/\text{cm}^2$ for 3-cm EMF and 60, 100 and 140 $\mu\text{W}/\text{cm}^2$ for 8-mm EMF. The biological activity of EMF was estimated by an integral D-parameter, which characterized the probability of normal functioning of an organism. The battery of tests conducted 1 mo after completion of EMF exposure included determinations of skin galvanic response, physical endurance, emotional stimulation, blood complement activity, plaque-formation, residual blood nitrogen concentration, cholinesterase activity, saturation of Fe-transferrin, cytochrome oxidase activities in liver and brain mitochondria, succinate dehydrogenase activity in brain mitochondria, and ceruloplasmin activity. Regression analysis indicated that 3-cm EMF produced more significant biological effects than 8-mm EMF. At an equal density and an equal duration of exposure, the 3-mm EMF were approximately sixfold more effective than the 8-mm EMF. These findings confirmed the biophysical data on the greater penetration of 3-cm EMF compared with that of 8-mm microwave radiation.

0515 EFFECT OF EXTREMELY-HIGH FREQUENCY ELECTROMAGNETIC FIELDS ON BACTERIA. (Rus.) Pedenko, A. I. (Dept. Nutrition, Hygiene and Microbiology, Inst. Public Nutrition, Kharkov, USSR); Belitskii, B. I.; Lerina, L. V.; Makeev, Yu. V.; Kutashov, V. N. *Izv Vyssh Ucheb Zaved Pishchev Tekhnol* (5):54-56; 1982 (no refs).

The sterilizing effect of extremely-high frequency (EHF) electromagnetic fields (EMF) was studied in suspensions of various bacteria. The EHF EMF were created by a continuous wave GZ-10A 2375 MHz generator with output power of 3 W. The viability of the irradiated cultures was compared to those of heated and intact suspensions. The viability of an *Escherichia coli* suspension after 30 sec to 20 min exposure to EHF EMF was 2-3 x lower than that after conventional heating to 29-56 °C. A complete sterilizing effect was achieved after 3-min exposure and a temperature of 46 °C. A similar decrease in viability after exposure to EHF EMF was observed in cultured *Staphylococcus*, *Pseudomonas aeruginosa* and sporogenous *Bacillus subtilis*.

0516 ROLE OF POLARIZATION AND RESONANCE IN EVAL-

CATION OF BIOLOGICAL EFFECTS OF ELECTROMAGNETIC RADIATION. (Rus.) Galkin, A. A. (no affiliation given). *Kosm Biol Aviakosm Med* 16(2):84-87; 1982 (16 refs).

To provide a more correct approach to the evaluation of biological effects of electromagnetic radiation (EMR), the relationships between the absorbed dose and polarization and resonance of the biological materials were analyzed. It was shown that a human body can be considered as a homogeneous ellipsoid of rotation and that this model provides a sufficiently accurate estimate of effective absorption surface. The parameter of relative absorption coefficient was shown to reflect the resonant properties of absorbed EMR by biological materials.

0517 EFFECT OF LOW-INTENSITY ELECTROMAGNETIC FIELDS ON HUMAN AND ANIMAL ERYTHROCYTES. (Rus.) Shabaev, V. P. (no affiliation given). *Kosm Biol Aviakosm Med* 16(3):91-92; 1982 (7 refs).

Biological effects of low-intensity electromagentic fields (EMF) were studied in suspensions of human and rat erythrocytes. The erythrocyte suspensions were stored in a lead housing that provided a 100-200-fold reduction of the Earth's EMF. The effects of Earth EMF were estimated by oxygen concentration in Ringer solution and by osmotic hemolysis. Erythrocyte suspensions stored in the shielding housing showed an increase in oxygen content (by 8% compared with that in erythrocytes exposed to the Earth's EMF). Electrophoresis of erythrocyte extracts showed the presence of three protein fractions, compared with one fraction in erythrocytes exposed to Earth EMF. It was suggested that the mechanism of the shielding effect is associated with changes in the structural characteristics of intracellular and extracellular water.

0518 CONSTANT LOW-FREQUENCY ELECTRIC AND ELECTROMAGNETIC FIELDS (BIOLOGICAL EFFECT, HYGIENE EVALUATION). (Rus.) Davydov, B. I. (no affiliation given); Karpov, V. N. *Kosm Biol Aviakosm Med* 16(5):18-25; 1982 (27 refs).

In an effort to establish the maximum permissible exposure levels for atmospheric electric and electromagnetic fields, literature data on the biological effects of low-frequency (LF) electromagnetic fields (EMF) are reviewed with special attention to the exposures of airplane pilots. The degree of biological activity of EMF is directly related to its frequency, the integral power of all sources of radiation, regimen of irradiation, duration of exposure, and the distance from the source of radiation. The dosimetric approach should be based upon relative biological effectiveness of absorbed energy for the entire spec-

trum. Marked increase of the specific conductivity of biological tissues after irradiation with frequencies of 10^4 - 10^5 Hz can be explained by chain-like involvement of intracellular water into ion formation. The energy of electromagnetic radiation absorbed by biological tissues is transformed into thermal energy. For frequencies up to 10 MHz, the size of a human body is small compared with the wavelength, so that the human body can be considered as a homogeneous ellipsoid conductor. Calculation of the levels of irradiation with EMF at frequencies of up to 3×10^8 Hz indicated that exposure to natural sources of EMF is relatively safe.

0519 PHYSICAL FACTORS OF THE ENVIRONMENT AS A HYGIENIC PROBLEM. (Rus.) Shandala, M. G. (A. N. Marzzeev Res. Inst. General and Community Hygiene, Kiev, USSR). *Vestn Akad Med Nauk SSSR* (1):9-16; 1981 (23 refs).

Potential public health hazards of mechanical, thermal, optical, electric, magnetic, electromagnetic and ionizing environmental factors are briefly discussed, with special emphasis on establishment of maximum permissible exposure levels (MPEL). The biological effects of a static electric field included reduced sensitivity to various stimuli, reduced skin blood supply, and inhibition of the reduction-oxidative processes in the skin. The MPEL of static electrical fields after chronic exposure was recommended at 20 kV/m. Biological activity of microwaves at thermal ($> 1 \text{ mW/cm}^2$) and nonthermal levels included changes in the nervous, cardiovascular, and immunological systems. Prolonged exposure to an industrial frequency electromagnetic field (50 Hz) induced changes in the functional state of the central nervous system, endocrine system, cardiovascular system, and reproductive system. The MPEL for industrial frequency electromagnetic fields was recommended at $< 1,000 \text{ V/m}$.

0520 BIOLOGICAL AND THERAPEUTIC EFFECTS OF MICROWAVES. (Rus.) Obrosov, A. N. (Central Res. Inst. Balneology and Physical Therapy, Moscow, USSR); Krylov, O. A. *Vopr Kurortol Fizioter Lech Fiz Kult* (2):1-8; 1982 (no refs).

Therapeutic applications and the mechanism of action of microwave (MW) radiation are reviewed. In Soviet literature, both decimeter-band waves (100-10 cm) and centimeter-band waves (10-1 cm) are classified as extremely-high frequency waves, while ultra-high frequency waves include only electromagnetic fields with a wavelength of 1-10 m. The effect of MW on biological materials includes a thermal component, which depends upon the power flux density, and a nonthermal or specific component. Most of the therapeutic applications of MW are based upon their thermal effects. MW are characterized by significant penetration and

absorption in the tissues and the thermal effects of MW are measured by total or local specific absorption rates. Absorption of MW energy also depends upon the orientation of the electric field, grounding, and reflecting surfaces. Irradiation of animals that have a system of active thermoregulation (dogs) was shown to produce less marked increase in brain temperature than the irradiation of animals that do not have a cooling system (rabbits). Decimeter-band waves with moderate power flux density (80 mW/cm^2) were found to reduce blood pressure, while MW with a higher power flux density (400 mW/cm^2) were found to induce gastroduodenal ulcers. Decimeter-band waves and sine-modulated currents were found to stimulate dopamine content in the cerebral cortex and in the caudate nucleus. Local irradiation of the adrenal glands or whole body irradiation at extremely low power flux density (1 mW/cm^2) stimulated release of glucocorticoids and thus inhibited the immune response. The nonthermal effects of MW radiation observed at relatively low power flux densities ($< 10 \text{ mW/cm}^2$) were associated with changes in the structure of intracellular water, and, in turn, with changes in protein conformation.

0521 EFFECT OF DECIMETER-BAND WAVES ON THE FUNCTIONAL STATE OF THE CARDIOVASCULAR SYSTEM AND VARIOUS IMMUNOLOGICAL AND BIOCHEMICAL INDICES IN PATIENTS WITH MYOCARDIAL INFARCTION DURING THE RECOVERY PHASE. (Rus.) Sorokina, E. I. (Central Res. Inst. Balneology and Physical Therapy, Moscow, USSR); Poshkus, N. B.; Tupitsina, Iu. Iu.; Volkova, L. P.; Shubina, A. V.; Krasnikov, V. E. *Vopr Kurortol Fizioter Lech Fiz Kult* (2):9-13; 1982 (9 refs).

Therapeutic efficacy of decimeter-band waves was studied in 142 men with myocardial infarction. The decimeter-band waves were produced by a Volna-2 generator (output power of 20 and 40 W). Of 142 patients, 101 received irradiation of the D_{I-V} region, 25 of the D_{II-IV} region, and 16 of the posterior surface of the shins. The patients received daily, 10-min radiation treatment (10-15 applications per treatment course). The recuperation period was complicated by angina pectoris attacks (79.6% of the patients) or by sporadic extrasystoles (75%). Favorable effects of decimeter-band waves included increase in the aerobic capacity of the heart, decrease in hypoxia zone (normalization of ST segment), improvement of energy metabolism, decrease in the titer of anticardial antibodies and IgG level, and decrease in enzyme activities. The best results were achieved after irradiation of the D_{I-V} region at 40 W.

0522 IMMUNOSUPPRESSIVE AND IMMUNOSTIMULATING EFFECTS OF DECIMETER-BAND WAVES DURING THE PRIMARY IMMUNE RESPONSE. (Rus.) Bogoliubov, V. M. (Central Res. Inst. Balneology and Physical Therapy, I. M. Mechnikov Res. Inst. Vaccines and Serums, Moscow,

USSR); Frenkel', I. D.; Pershin, S. B.; Ponomarev, Iu. T.; Sokolova, Z. A.; Zubkova, S. M.; Kuz'min, S. N.; Galenchik, A. I.; Kozlova, N. N. *Vopr Kurortol Fizioter Lech Fiz Kult* (2):13-17; 1982 (10 refs).

Immunological effects of decimeter-band waves (DBW) were studied in male rabbits immunized with thymus-dependent antigen of sheep erythrocytes. The 460 MHz DBW were generated by a Volna-1 apparatus with a contact ceramic irradiator (4 cm in diameter) at power flux density of 120 mW/cm². The animals were irradiated for 6 min/day for 10 days. Group 1 was irradiated in the thyroid gland region and Group 2 in the adrenal gland regions. The animals were immunized after two or six exposures, or on day 10 after completion of irradiations. The immune response was estimated by the number of antibody-forming cells in the spleen and by a titer of serum hemagglutinins. The effect of DBW on the primary immune response depended upon the site of irradiation and the time period between irradiation and immunization. Irradiation of the thyroid gland region during the induction of immune response had an immunosuppressive effect, while irradiation 10 days prior to antigen administration had an immunostimulating effect. In contrast, irradiation of the adrenal gland regions produced inhibition of the immune response, regardless of the timing of antigen administration.

0523 EFFECT OF DECIMETER-BAND WAVES ON TEMPERATURE OF THE BRAIN AND THE ADJACENT TISSUES (EXPERIMENTAL STUDY). (Rus.) Malikova, S. N. (Experimental Dept., Central Res. Inst. Balneology and Physical Therapy, Moscow, USSR); Malyshev, V. L.; Balakireva, V. N.; Gorban', L. G. *Vopr Kurortol Fizioter Lech Fiz Kult* (2):18-25; 1982 (4 refs).

The effects of decimeter-band waves (DBW) on body temperature regulation were studied in phantoms, rabbits, and dogs. The DBW were generated by Romashka and Ranet apparatuses with contact irradiators (40 mm in diameter), output power of 5, 15, and 25 W, and power flux density of 400, 1200, and 2000 mW/cm², respectively. The site of irradiation was the parieto-temporal region. The temperature of the brain and the adjacent tissues was measured by a thermocouple. In the phantom, temperature was measured at depths of 5, 15, 20, 25, and up to 50 mm; temperature was found to decrease with depth. Increased duration of exposure was associated with increased heat emission and thus with a decrease in the rate of temperature gain. Measurements of brain and skin temperature in rabbits and dogs indicated that increases in temperature depended upon distance from the DBW source, duration of exposure, and the power flux density. The increase in brain temperature in rabbits was significantly more pronounced than in dogs.

0524 EFFECTS OF DECIMETER-BAND WAVES AND SINE-MODULATED CURRENTS ON NUCLEAR DNA CONTENT IN BRAIN NEURONS (EXPERIMENTAL STUDY). (Rus.) Mikhailik, L. V. (Lab. Physiology, Experimental Dept., Central Res. Inst. Balneology and Physical Therapy, Moscow, USSR). *Vopr Kurortol Fizioter Lech Fiz Kult* (2):22-25; 1982 (7 refs).

The effects of decimeter-band waves (DBW) alone and in combination with sine-modulated currents (SMC) on DNA content in sensorymotor cortex and caudate nucleus neurons were studied in male Wistar rats. DBW were generated by a Volna-1 apparatus with a 4-cm irradiator at a power flux density of 110 mW/cm² (3 min/day, for 10 days). SMC were generated by an Amplipulse-3 apparatus (30 Hz, carrier frequency of 5 kHz, 100% modulation, 2-3 mA current; 20 min/day, for 20 days). The DBW were applied to the head and SMC were applied to the femur region. Combined exposure consisted of irradiations with SMC for the first 10 days, followed by DBW for 3 min and SMC for 20 min during the next 10 days. DNA content was measured cytospectrophotometrically. Single and repeated applications of DBW did not affect DNA distribution in the sensorymotor cortex and caudate nucleus neurons. Single applications of SMC also did not affect DNA content in the neurons. Repeated applications of SMC resulted in a significant increase in DNA content in the neurons of the sensorymotor cortex, while DNA content in the neurons of the caudate nucleus did not differ from that in controls. Combined exposure to DBW and SMC enhanced polyploidization of neurons of the sensorymotor cortex (DNA content of 3.96 units, compared with 3.39 units in controls) and to a lesser degree of the neurons of the caudate nucleus (3.44 units, compared with 3.16 units in controls).

0525 THE EFFECT OF BRAIN IRRADIATION WITH DECIMETER-BAND WAVES ON AUTONOMIC FUNCTIONS IN HYPERTENSION (EXPERIMENTAL STUDY). (Rus.) Golinskaya, M. S. (no affiliation given). *Vopr Kurortol Fizioter Lech Fiz Kult* (2):25-28; 1982 (8 refs).

The effects of decimeter-band waves (DBW: wavelength of 65 cm) on the autonomic nervous system were studied in Wistar rats with immobilization-induced hypertension. DBW were generated by Romashka and G-4-37A apparatuses (power flux density of 80 and 400 mW/cm²). The functional activity of the autonomic nervous system was evaluated by motor activity, maximum blood pressure, heart rate, and energy metabolism. Irradiations of the brain region with DBW resulted in decreased blood pressure (130 and 108 mm Hg after exposure to 80 and 400 mW/cm², respectively, compared with 158 mm Hg in controls). The decrease in blood pressure after irradiation at 80 mW/cm² was associated with mild inhibition of motor activity, decrease in energy metabolism, and decrease in heart and respiration rates. Irradiations at higher power flux density (400 mW/cm²) produced hemorrhages in the myocardium, brain, and small intestine mucosa, disorders of the

atrioventricular conduction, and marked inhibition of energy metabolism (7/20 rats died after the seventh irradiation). These findings indicate that the use of DBW in the treatment of hypertension should be limited to irradiations at low power flux density.

0526 DECI-METER-BAND WAVES IN COMBINED TREATMENT OF PATIENTS WITH INSUFFICIENCY OF CEREBRAL CIRCULATION. (Rus.) Strelkova, N. I. (Central Res. Inst. Balneology and Physical Therapy, Moscow, USSR). Vopr Kurortol Fizioter Lech Fiz Kult (2):28-31; 1982 (11 refs).

Therapeutic efficacy of decimeter-band waves (DBW) was evaluated in patients with Parkinson's disease (Group 1), in patients with complications of brain injuries (Group 2), in patients with spastic hemiparesis due to cerebral ischemia (Group 3), and in patients with transient cerebral ischemia (Group 4). The DBW were generated by a Volna-2 apparatus. The output power was 20-40 W in Group 1, 20-30 W in Groups 2 and 3, and 20 W in Group 4. The patients received daily, 10-15-min irradiations (10-15 applications per treatment course). Exposures to DBW resulted in marked improvement of cerebral circulation, formation of collateral circulation, and improvement of dopamine metabolism. Irradiations of the cervical region were more effective than irradiations of the occipital region.

0527 EXPOSURE TO CENTIMETER-BAND WAVES WITH SUBSEQUENT ELECTROPHORESIS OF NICOTINIC ACID IN COMBINED TREATMENT OF PATIENTS WITH COMPLICATIONS OF VIRAL ENCEPHALITIS. (Rus.) Ezhova, V. A. (Res. Inst. Physical Therapy and Medical Climatology, Yalta, USSR); Kunitsina, L. A.; Kornienko, E. G.; Leshchinskaya, N. P.; Cherfus, I. S.; Guz, S. Ia. Vopr Kurortol Fizioter Lech Fiz Kult (2):32-35; 1982 (8 refs).

Therapeutic efficacy of centimeter-band electromagnetic fields alone and in combination with electrophoresis of nicotinic acid was studied in 200 patients (80 men, 120 women; 20-40 yr old) with complications of viral encephalitis. All patients had manifestations of cerebral circulation disorders. The centimeter-band waves were generated by an apparatus Luch-58 (output power of 20-40 W). Electrophoresis of nicotinic acid was carried out by sine-modulated current (5000 Hz, 10-15 mA current, 0 modulation): the active electrode was placed in the region of the C_{VII}-VIII and D_I-III vertebrae and the second electrode was placed on the extensor surface of the right forearm. One hundred patients were exposed to the centimeter-band waves in combination with nicotinic acid electrophoresis and 50 patients received irradiations with centimeter-band waves alone (controls). Combined treatment resulted in marked improvement of clinical and neurological symptoms: headache disappeared in

57% of the patients (compared with 46% of controls), 65% stopped complaining of dizziness (versus 52% of controls), 71% showed normalization of sleep (versus 58% of controls). Normalization of rheoencephnolagraphic indices was observed in 80% of the patients who received combined treatment and in 68% of controls. Combined treatment resulted in normalization of blood heparin level and in normalization of the urinary excretion of catecholamines.

0528 EFFECT OF DECI-METER-BAND WAVES ON IMMUNOLOGIC REACTIVITY OF PATIENTS WITH OSTEOARTHROSIS DEFORMANS. (Rus.) Dalimov, Z. A. (Dept. Physical Therapy and Balneology, Inst. Advanced Training for Physicians, Tashkent, USSR); Alimova, M. Iu. Vopr Kurortol Fizioter Lech Fiz Kult (2):51-52; 1982 (no refs).

The effects of decimeter-band electromagnetic field (DB EMF) on indices of non-specific immunity were investigated in 60 patients (22 men, 38 women; 35-65 yr old) with osteoarthritis deformans. The DB EMF was generated by a Volna-2 apparatus (output power of 40-50 W). The patients received daily 8-10-min irradiations of the involved joints (a total of 16-20 irradiations). The DB EMF treatment produced local analgesic effect in 80% of the patients, reduced intensity of inflammation in 72%, and improved the peripheral circulation in 74%. Two-thirds of the patients showed normalization of blood protein fractions, decrease of C-reactive protein concentration (from 1.47 to 1.02 units), and decrease in erythrocyte sedimentation rate (from 28 to 16). Treatment with DB EMF produced significant decrease in the titers of autoantibodies to the synovial membranes, to the heart, tonsils, kidneys, liver, and spleen. These findings were indicative of a high efficacy of DB EMF in combined treatment of patients with osteoarthritis deformans.

0529 DECI-METER-BAND THERAPY WITH THE USE OF TRANSPORTABLE APPARATUSES. (Rus.) Shurikhina, L. A. (Central Res. Inst. Balneology and Physical Therapy, All-Union Res. Center for Motherhood and Childhood Protection, N. N. Burdenko Chief Military Clinical Hosp., Moscow, USSR); Strugatskii, V. M.; Ushakov, A. A. Vopr Kurortol Fizioter Lech Fiz Kult (2):68-69; 1982 (no refs).

Therapeutic applications of Romashka and Ranet (DMV-20) transportable apparatuses generating decimeter-band waves (460 MHz, wavelength 65 cm) are described. Characteristic features of these apparatuses include relatively low output power (17-20 W) and relatively small size of the contact irradiators (20, 40, and 100 mm); the 20-mm irradiator is used for intravaginal applications, while the 40-mm and 100-mm irradiators are applied to the skin. The transportable decimeter-band wave generators are effective in the treat-

ment of bronchial asthma, nonspecific bronchopulmonary diseases in children, stomach and duodenal ulcer, neuralgia of the trigeminal nerve, acute neuritis of the facial nerve, lumbosacral radiculitis, subacute and chronic pyelonephritis, subacute and chronic uterine inflammations, hematoma, tonsillitis, otitis, inflammation of the maxillary and frontal sinuses, furunculosis, and prostatitis.

0530 SPECIFIC EFFECTS OF MILLIMETER-BAND RADIO WAVES ON BIOLOGICAL SYSTEMS. (Rus.) Sevast'ianova, L. A. (no affiliation given). In: Nonthermal Effects of Millimeter-band Radiation. Deviatkov, N. D., ed. (Moscow: USSR Acad. Sciences): pp. 86-113; 1981 (23 refs.).

Literature data on the specific biological effects of millimeter-band radio waves (RW) are reviewed. Biological changes induced after exposure to millimeter-band RW were found to depend upon the wavelength, the threshold power flux density, and duration of exposure. Numerous experiments showed the resonant-type relationship between the wavelength and the biological effect. Approximately 70% of the energy of millimeter-band RW was absorbed in the tissues at a depth of 300 microns. Millimeter-band RW had a selective effect on bone marrow cells: exposure to RW prior to x-irradiation was found to have a radioprotective effect on medullary hematopoiesis, while exposure to RW after x-irradiation was found to have a radiosensitizing effect. Millimeter-band RW in combination with x-rays and antineoplastic agents enhanced the inhibition of tumor growth and reduced radiation injuries to the bone marrow.

0531 EFFECT OF MILLIMETER-BAND ELECTROMAGNETIC WAVES ON BACTERIAL CELLS. (Rus.) Smolianskaya, A. Z. (no affiliation given). In: Nonthermal Effects of Millimeter-band Radiation. Deviatkov, N. D., ed. (Moscow: USSR Acad. Sciences): pp. 132-146; 1981 (24 refs.).

The results of experiments on the biological effects of millimeter-band electromagnetic fields (EMF) on bacterial cells are reported. Analysis of induction of lethal colicin synthesis in *Escherichia coli* K12 C 600 after exposure to 5.8-7.1-mm EMF showed the resonant relationship between the wavelength and the number of colicin-synthesizing bacteria. The effect was directly related to the duration of exposure and was independent of the power flux density. The millimeter-band had a similar effect on the inducible synthesis of beta-galactosidase in lysogenic *Staphylococcus aureus*. These findings indicate that the lethal effects of millimeter-band EMF were associated not with direct thermal action but rather with indirect action mediated through resonant stimulation of bacterial systems.

0532 EFFECT OF MILLIMETER-BAND RADIO WAVES ON TUMOR GROWTH IN EXPERIMENTAL ANIMALS. (Rus.) Sevast'ianova, L. A. (no affiliation given); Borodkina, A. G.; Golant, M. B.; Rebrova, T. B. In: Nonthermal Effects of Millimeter-band Radiation. Deviatkov, N. D., ed. (Moscow: USSR Acad. Sciences): pp. 147-166; 1981 (19 refs.).

Therapeutic efficacy of millimeter-band radio waves (MB RW) in combination with x-rays or antineoplastic agents was studied in male rats with sarcoma-45, male random-bred mice with sarcoma-180, and female CBA mice with transplanted cervix carcinoma CC-2. The animals with sarcoma-45 and CC-2 were exposed to MB RW (wavelength of 7.11 mm, power flux density of 12.5 mW/cm², for 1 hr) and to x-rays (total dose 2,100 rads). Exposure to MB RW following x-irradiation resulted in a 2.5-fold increase in the inhibition of sarcoma-45 growth over that after x-irradiation alone. Exposure to MB RW before x-rays did not enhance the inhibitory effect of irradiation. Inhibition of CC-2 growth after exposure to x-rays followed by MB RW was twofold greater than after exposure to x-rays alone. Exposure to MB RW before x-irradiation prevented radiation injuries to the bone marrow and the peripheral blood in the animals with sarcoma-45 and CC-2. MB RW after x-irradiation failed to provide a radioprotective effect. MB RW enhanced the antitumor activity and reduced the toxicity of cyclophosphamide and flotafur in mice with sarcoma-180.

0533 ENHANCED LIPID PEROXIDATION IN LIPOSOMES AFTER EXPOSURE TO MILLIMETER-BAND RADIATION. (Rus.) Andreev, V. E. (no affiliation given); Betskii, O. V.; Il'ina, S. A.; Kazarinov, K. D.; Putvinskii, A. V.; Sharov, V. S. In: Nonthermal Effects of Millimeter-band Radiation. Deviatkov, N. D., ed. (Moscow: USSR Acad. Sciences): pp. 167-176; 1981 (23 refs.).

Nonthermal effects of millimeter-band electromagnetic fields (MB EMF) on biological membranes were investigated. The rate of lipid peroxidation after exposure to 7.1-4.7-mm (42-64 GHz) waves was studied in phospholipid liposomes. Lipid peroxidation was initiated by addition of iron sulfate + ascorbic acid mixture, by ultraviolet irradiation, and by irradiation with visible light. MB EMF resulted in a 20-30% increase in the rate of lipid peroxidation. The enhanced rate of peroxidation was observed for all three types of initiation and for all wavelengths tested. The mechanism of MB EMF-induced increase in the rate of lipid peroxidation could be associated with free radical processes in the membranes, with structural changes in the liposome membranes, or with changes in diffusion of peroxidation substrates and products.

MEETING ABSTRACTS

0534 NATURAL RADIOFREQUENCY ELECTRICAL OSCILLATIONS IN THE LIVING STATE (MEETING ABSTRACT). (Eng.) Pohl, H. A. (Oklahoma State Univ., Stillwater, OK 74078). Abstracts of Papers of the American Chemical Society 183(March):A14; 1982.

The research of this laboratory has recently shown that cells emit radiofrequency (RF) electric fields, especially at or during mitosis. This is observed in bacteria, in yeasts, in algae, in avian cells, and in mammalian fetal, normal, and oncogenic fibroblasts; and hence is probably "universal". For some years we have been using non-uniform electric fields to manipulate and examine cells by the phenomenon of dielectrophoresis. (The pull of neutral particles exerted by a non-uniform electric field.) From these gentle dielectrophoresis effects one can obtain unique dielectric relaxation spectra and also sort cells. In a recent turnabout, we used the phenomenon of dielectrophoresis to study the oscillating fields of cells themselves, as evidenced in two fundamental ways. We observe that the natural RF fields of cells produce an attraction for tiny and highly polarizable particles ("magic" particles), and ignore "non-magic" particles of low polarizability. These simple and direct experiments demonstrating natural RF fields from cells require little more than a microscope and a knowledge of what to do. In a second technique, these observations were supplemented by showing that living cells spin in a resonant manner in response to narrow frequency ranges (Cellular Spin Resonance). The CSR spectra and the micro-dielectrophoresis studies were a direct outcome of the theories of H. Frohlich. Our model for these natural RF oscillations of nucleate cells is that of charge-density waves arising from the ionic phases of periodic intracellular reactions, operating in collective coherence, and collimated by intra-cellular structures to form the externally observable oscillating fields.

0535 EFFECTS OF INDUCED ELECTROMAGNETIC FIELDS ON HORMONAL RESPONSIVENESS OF OSTEOBLASTS IN VITRO (MEETING ABSTRACT). Luben, R. A. (Div. Biomedical Sciences and Dept. of Biochemistry, Univ. California, Riverside, CA 92521); Cain C. D. Abstracts of Papers of the American Chemical Society 183(March): A15; 1982.

Pulsing electromagnetic fields are known to significantly improve the healing of bone fractures *in vivo*. The current study was designed to investigate the molecular basis of the actions of these fields on bone, by using bone and bone cells cultured *in vitro*. Mouse osteoblasts (cell line MMB-1) were exposed in culture to fields produced by devices currently approved for clinical use ("Bi-Osteogen"). These fields produced little or no change in basal activities in the cells, but significantly inhibited the cAMP responses of the cells to added parathyroid hormone (PTH) or osteoclast activating factor (DAF). The effects of PTH on syn-

thesis of collagen were also blocked by the fields. However, the fields had no effects on activities of vitamin D derivatives in the cells, suggesting that only hormones acting at the cell membrane were affected. The inhibition of cAMP responses was mediated by reductions in the activity of PTH-activated adenylyl cyclase in cell membrane preparations; however, the fields had no effect on the total fluoride-activated adenylyl cyclase activity in the same fractions, indicating that the effects were localized either to the hormone receptor or the receptor-cyclase coupling moieties of the cell membrane. Similar effects of the fields were observed using intact mouse cranial bones in organ culture. The results suggest that the effects of electromagnetic fields on bone are at least partially mediated by modification of the responses of the cells to endogenous hormones, and that the stimulation of bone formation *in vivo* by these fields is the result of localized blocking of the osteolytic effects of PTH.

0536 EFFECTS OF ELECTRIC FIELDS ON NEURITE GROWTH IN VITRO (MEETING ABSTRACT). (Eng.) Poo, M.-M. (Dept. Physiology & Biophysics, Univ. California, Irvine, CA 92717); Patel, N. Abstracts of Papers of the American Chemical Society 183(March): A16; 1982 (4 refs).

The effect of DC fields on neurite growth in culture has been a controversial subject over many decades. Recent investigations on cultured ganglionic explants and on dissociated single embryonic neurons have provided convincing evidence that DC fields on the order of 0.1 to 10 V/cm could produce at least three types of effects on neuronal growth: (1) accelerated growth of the neurites facing the cathode, (2) bending and orientation of the neurite tip toward the cathode, (3) general enhancement of neurite outgrowth from the soma and the survival of the neuron in culture. Furthermore, the effects are not due to secondary mechanical or chemical factors in the growth environment of the neuron. Rather, the electric field exerts its action directly on the neuron. Since similar fields produced electrophoretic accumulation of cell surface glycoproteins on the cathodal side of the neuron, the field-induced reorganization of plasma membrane components could be a cellular mechanism underlying the electric field effects on neuronal growth.

0537 SYNERGY OF POLYMER IMMUNOMODULATION AND PULSATILE ELECTROMAGNETICALLY INDUCED CURRENTS IN INHIBITION OF GROWTH OF MURINE MALIGNANT MELANOMA (MEETING ABSTRACT). (Eng.) Norton, L. (Mount Sinai Sch. Medicine, New York, NY); Tansman, L. S.; Regelson, W.; Geller, S.; Pilla, A. A. Abstracts of Papers of the American Chemical Society 183(March): A17; 1982.

Meeting Abstracts

Biological Effects of Nonionizing Electromagnetic
Radiation Vol 2-4 July 1983

We have reported that pulsating electromagnetic-induced current (PEMIC), designed to modulate membrane enzyme kinetics, has anti-cancer activity in B16 melanoma in mice, acting synergistically with cytotoxic combination chemotherapy. In this work it is shown that PEMIC and Pyran co-polymer, an immunomodulating drug, are effective tumor growth inhibitors with combined use. 110 female BDF₁ or SCF₁ mice were given no drug or Pyran, 75 mg/kg, 1 or 7 days after implantation of 1 mm³ B16 melanoma. PEMIC treated mice were placed in specially constructed cages between Helmholtz air-gap coils for 10 hr/day. The pulsating magnetic field (48 da = 0.1 G used) induced 1 Hz currents configured of 50 msec bursts of 150 usec main polarity and + usec opposite polarity assymetrical pulses. The average induced current per pulse varied from 1.4 - 1.6 A cm⁻². The results show that the median survival time for control animals of seven wk was not affected by PEMIC or Pyran alone. However, treatment with PEMIC and Pyran increased survival time to 11 wk in 100% of the mice. Histologic studies showed enhanced necrosis for PEMIC treated tumors, suggesting a mechanism of synergy with the macrophage and NK-cell stimulating Pyran. These results provide evidence for an effective and non-toxic anti-cancer treatment modality.

1508 EFFECTS OF WEAK PULSATING CURRENT ON VITALITY IN PARAMECIUM (MEETING ABSTRACT). Eng. J. Smith-Sonneborn, J. (Zoology & Physiology Dept., Univ. Wyoming, Laramie, WY 82071). Abstracts of Papers of the American Chemical Society 183(March 1982).

Since the surface membrane of the ciliated protozoan Paramecium exhibits properties of excitability which mimic metazoan nerve and muscle cells, this eukaryote has been used extensively for studies of membrane excitation and motor behavior. The biological effects of specific pulsating current on these cells was investigated using electromagnetic current induction in the expectation that these cells would respond to proper electrochemical stimulation. The induced voltage was obtained using air-gap coils driven by a programmable power supply (Electro-Biology Inc., Fairfield, NJ). The basic pulse wave form is bipolar and assymetrical in width and amplitude usually in a ratio of 1:10. Periodicity of the wave form single pulse versus burst and repetition rate was examined. The response of the cells to specific pulsating current with respect to: 1) their daily cell division rate and 2) duration of lifespan was monitored. Paramecium have been used as a model system of cellular senescence since the number of cell divisions after origin at fertilization until death is limited, predictable and species-specific and therefore can be used to study effects on longevity. Specific pulsating currents and ionic environments were found to increase the rate of cell division and duration of lifespan.

1509 NON-EQUILIBRIUM MODELS OF CELL MEMBRANE INTERACTIONS WITH WEAK ELECTROMAGNETIC FIELDS (MEETING ABSTRACT). Eng. Eng. V. R. Lima Linda VA Hosp., CA 91357. Abstracts of Papers of the American Chemical Society 183(March 1982).

Studies in various tissues, including cerebral cortex and synaptosomal fractions, cultured osteoblasts, prototoxic T-lymphocytes and pancreatic islets, offer good evidence that coupling of weak, oscillating electrochemical fields to cell membranes occurs on membrane surface polyvalents, characterized by transient coherent states of nearest neighbor fixed-energy sites. First steps in transductive coupling may occur in the length of the membrane surface where different states may exist for considerable distances. Binding and release of calcium ions at these receptor sites correlates closely with exposure to certain weak electromagnetic fields. Sensitivity to these fields in narrow frequency and amplitude "windows" supports models based on highly cooperative dissipative interactions at cell membrane surface glycoproteins. Reaction-diffusion-dispersive soliton processes may also be involved. Soliton waves may arise from interactions with phonons and excitons along linear molecules producing nonlinear molecular vibrations. Solitons exist in a minimal energy state and are extremely long-lived in comparison to linear oscillations. They may also couple reaction-diffusion processes in the extracellular and intracellular domains. Calcium fluxes in the extracellular space of the central nervous system are considered as a non-linear reaction-diffusion system. Solitons in membrane long-chain molecules (Davydov type) may be significant in charge transfer or conver energy as nonlinear waves along gelid domains from one protein site to another Sine-Gordon soliton.

1510 THE EFFECT OF MICROWAVE IRRADIATION ON THE tRNA-SYNTETASE SYSTEM OF THE CHICK BRAIN AND LIVER (MEETING ABSTRACT). Eng. Dr. E. B. "Frederic Joliet-Curie" Natl. Res. Inst. of Radiobiology and Radionuclides, H-1175 Budapest, H-1055, Hungary; Bélaiv, L.; Szabó, L. I. Acta Physiol Hung 17(1-2):130; 1981.

The biological effect of microwave irradiation in embryonic organisms of higher radiosensitivity has been studied. White Leghorn chick embryos were incubated at 37.5°C at a relative moisture of 100%. Continuous irradiation (CW) was brought about with a power density range between 100-300 mW/cm² in a frequency of 2450±50 MHz. We have found that embryos irradiated at different days of the embryo life between the 2nd and 19th day of incubation, with various power density ranges showed differences both in their survival and characteristics of the development as well as in their radiosensitivity. We have found that the radiosensitivity increases reciprocally with the age of the embryo. Effect of the microwave lift radiation on the embryonic protein synthesis was in-

vestigated with a specific absorption of 220 mW/g at the 15th day of embryonic life. In order to compare some macromolecules taking part in protein synthesis, tRNAs and aminoacyl tRNA synthetases were isolated from the brain and the liver of chicken embryos irradiated at the 15th day. tRNAs' acceptor activity and enzyme activity of synthetases showed a small decrease in liver, and about 50% increase in brain. The activity of tRNA seems to be more sensitive than that of the synthetases.

0541 RADIOPHREQUENCY ELECTROMAGNETIC FIELDS AS A RISK FACTOR IN DIFFERENT PROFESSIONAL GROUPS IN BULGARIA (MEETING ABSTRACT). (Eng.) Dobrev, B. (Inst. Hygiene, Bul. D. Nestorov N 15, Sofia 1431, Bulgaria); Israel, M. S.; Todorova, L. C. J Occup Accidents 4(2-4):187; 1982.

The intensity of electromagnetic fields (EMF) have been measured in industrial enterprises, radio and TV stations, medical establishments, high frequency telecommunication stations, electronic industry, radar installations, scientific institutes etc., in connection with the application of new technologies. EMF intensities (or power density) in the machine and metal processing industry, in physiotherapy, in some of the radio transmitting stations, in the plastics industry, in some scientific institutes, are higher than the occupational health norms in Bulgaria. Clinical, functional, paraclinical, biochemical and immunological investigations have been performed on 390 workers in order to define the effect of electromagnetic fields in working conditions. Electromagnetic fields have been found to cause a health hazard in the machine building industry - 28.6% of the examined workers, in the plastics industry - 31% (machine workers), at high frequency telecommunications stations - 71%, in the metal processing and metallurgical industries - 15.1% of the workers.

0542 MEASUREMENTS OF THE INTENSITY OF RADIOPHREQUENCY ELECTROMAGNETIC FIELDS AS A RISK FACTOR IN BULGARIA (MEETING ABSTRACT). (Eng.) Israel, M. S. (Inst. Hygiene and Occupational Health, Bul. D. Nestorov N 15, Sofia 1431, Bulgaria). J Occup Accidents 4(2-4):189; 1982.

The measurement of the intensity of the electromagnetic fields (EMF) in working rooms is connected with many difficulties: EMFs are very intensive, the workplaces are near to grounding metal masses, in the room there are reflected surfaces, etc. There are no apparatuses (serial production) with the necessary characteristics about the purposes for such measurements. The attempt to create and construct devices for measuring the EMFs in the frequency range below 30 MHz is described in the report and also the questions and problems which should be resolved in the

future. We construct antennas for measuring the intensities of the EMFs below 30 MHz with an accuracy of 10.5-12%.

0543 EFFECT OF MICROWAVE-INDUCED WHOLE-BODY HYPERTERMIA ON THE MUCOSA OF MOUSE SMALL INTESTINE (MEETING ABSTRACT). (Eng.) Tsubouchi, S. (Fukui Medical Univ., Matsusaka, Nagoya, Japan); Nishimoto, Y.; Kano, E.; Nakamura, W. J Radiat Res (Tokyo) 23(1):14; 1982.

Effect of microwave-induced whole-body hyperthermia was examined using ddY/SLC mice for the basic understandings of the critical organs. The treatment at 43.5°C for 20 min resulted in the mortality rate of 30-40% within day one. The surviving mice showed no specific disease. Preliminary autopsy examination showed that a considerable amount of the body fluid had leaked into intestinal lumen due to the transitory denudation of the epithelial cells of the small intestine villi within 3 hr, whereas epithelial cells of the crypts appeared intact until these cells of villi were completely denuded. After 4-9 hr, cryptal epithelial cells regenerated in some of the animals which probably could have survived for at least more than one day if they had not been sacrificed. The histology of the mice that died within one day suggested that the complete denudation of the villus epithelial cells might be the initial cause of death. These preliminary results suggest the following: 1) one of the critical target organs of the whole-body hyperthermia is mucosa of the small intestine; 2) whole-body hyperthermia affects the epithelial cells of intestinal villi whereas those of the crypts were not injured; in contrast, radiation effect is mainly given on the proliferative epithelial cells, i.e., of the crypts.

0544 CHANGES OF HEMATOCRIT, SODIUM AND POTASSIUM ION CONCENTRATION IN PLASMA INDUCED BY WHOLE-BODY HYPERTERMIA (MEETING ABSTRACT). (Eng.) Ohtsuka, K. (Aichi Cancer Center Res. Inst., Nagoya, Japan); Nakamura, W. J Radiat Res (Tokyo) 23(1):16; 1982.

The physiological effects of whole-body hyperthermia on animals and normal tissues are not well-known. In this report, we investigated the changes of hematocrit, sodium and potassium concentration in plasma and water content in small intestine of mouse induced by whole-body hyperthermia (43.5°C; 15, 20, 25, 30 min) with 2450 MHz microwave. Water content in the small intestine increased gradually after the hyperthermic treatment. It might result from leakage of blood components into the intestinal tract and inhibition of reabsorption of water due to intestinal lesion by the treatment. Hematocrit also increased after the treatment; there was a very high correla-

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tion between these two values. The longer the time of the treatment, the more the mice died. While the change of potassium concentration in plasma was small, sodium ion concentration of agonal or dead mice were more than twice of normal value. Moreover, erythrocytes of hyperthermia-treated mice were more fragile than those of non-treated control. From these results, it was suggested that abnormally high concentration of plasma sodium, which leaked out mainly from erythrocytes, was one of the lethal factors.

0545 COMBINED EFFECT OF SYSTEMIC HYPERTHERMIA AND MITOMYCIN C ON INTRAMUSCULARLY TRANSPLANTED TUMOR (MEETING ABSTRACT). (Eng.) Nakamura, W. (Aichi Cancer Center, Nagoya, Japan); Nishimoto, Y.; Nakayama, T. J Radiat Res (Tokyo) 23(1):16; 1982.

Tumor cells were of a cloned cell line FMA3 which were derived from Furth's mastocytoma and kept as ascites type by serial transplantation into the abdominal cavity LAF₁ mice. The cells in logarithmic growth were transplanted into right hind leg muscles of 9-12 wk-old mice. Treatments with 2450 MHz-wave alone, with Mitomycin C alone or with both in combination were started two days after the transplantation. Among several protocols examined, the most promising one was the daily systemic hyperthermia (rectal temperature of 42°C for 5 min for 5 days) which was used in combination with a single injection of 20 µg Mitomycin C 10 min prior to the first heat treatment. Two sessions of the combination carried out with an interval of one wk significantly suppressed not only tumor growth at the site of the transplantation but also the metastases in the lungs, liver, spleen and other tissues.

0546 EFFECT OF TRENTAL ON HYPERTHERMIA-INDUCED THROMBOCYTOSIS IN MICE (MEETING ABSTRACT). (Eng.) Nakayama, T. (Aichi Cancer Center, Nagoya, Japan); Nakamura, W. J Radiat Res (Tokyo) 23(1):16; 1982.

Effect of pre- or post-treatment of mice with 1,5 (oxohexyl) theobromine (Trental) on the hyperthermia-induced thrombocytosis was studied. Systemic hyperthermia was induced in mice by exposing them to 2450 MHz-wave and by controlling the electric power automatically with the use of a thermocouple inserted into the rectum as a sensor. The rectal temperature was kept at 43.5°C for 10 min. In these mice, the thrombocyte count decreased gradually reaching its minimal level in about 3.5 hr. Thereafter, it increased and returned to the initial level in 2.5 hr and reached the maximum level 2 or 3 days after the heating which was 2.3 times higher than normal. Injection of Trental was carried out immediately before or after the heating and was effective in preventing the occur-

rence of thrombocytopenia as well as that of thrombocytosis.

0547 FOCUSING OF THE 915 MHZ ELECTROMAGNETIC POWER IN DEEP HUMAN TISSUES: A MATHEMATICAL MODEL STUDY (MEETING ABSTRACT). (Eng.) Arcangeli, G. (Istituto Medico e di Ricerca Scientifica, 00191 Rome, Italy); Lombardini, P. P.; Lovisolo, G.; Marsiglia, G.; Piattelli, M. Strahlentherapie 158(6):378; 1982.

Most of the external microwave or radiofrequency applicators for local hyperthermia induce maximum heating on the tissue surface with a progressive temperature decrease with depth. The resulting temperature gradient does not allow a homogeneous heating to lesions deeper than 3-4 cm with a single applicator, even if skin cooling is used. However, deep heating could be achieved by an array of applicators. The difficulty of understanding microwave propagation within the human body is due to the numerous discontinuities favoring microwave scattering. The resulting electromagnetic field exhibits an intensity, a phase and a polarization varying dramatically from point to point. In this work, we have studied the behavior of the electromagnetic field in an adult man thorax section. This section, obtained by a CAT scan at the level of fifth thoracic vertebra, was ideally subdivided in 235 sub-volumes with dimensions non-inferior to the diffraction limit. Values of dielectric constant and conductivity, as measured in the laboratory, were attributed to each sub-volume. In our model, a peripheral array of 50 equidistant cooled, water-loaded, contacting antennae at 915 MHz, having an equal intensity and an externally controllable phase, have been assumed as microwave sources. The integral equation matrix method has been used for the calculation. As a result, a system of 3x235 scalar linear complex equations, which have been solved numerically, was obtained. In this study, the possibility of focusing ohmic power in a given point deep in the body has been tested, ignoring the thermodynamic problem, and the following results have been obtained: 1) Focusing of 915 MHz power in deep points is always possible, but it is generally associated by concentration of ohmic power also in other, unwanted points. The unwanted power may exceed that delivered in the focus; 2) however, it is possible to find antenna phase configurations, capable of lowering the unwanted powers below that at the focused level. These configurations can be determined by applying minimization methods.

0548 NON-LINEAR EFFECTS IN THE ELECTROMAGNETIC HEATING OF LIVING TISSUES (MEETING ABSTRACT). (Eng.) Bardati, F. (Istituto di Elettronica dell'Università di Roma, Italy); Gerosa, G. Strahlentherapie 158(6):378; 1982.

The problem of electromagnetic heating of living tissues has been considered, with reference to local microwave-induced hyperthermia for cancer therapy. In order to investigate theoretically the temperature distribution, a mathematical model of the living tissue has been specified before solving the thermal boundary value problem. The model takes into account the complicated thermal phenomena of the living tissue, namely metabolic heat generation and heat exchange with blood flow. We have assumed a time-independent metabolic heat generation to be present. The cooling effect due to blood flow has been assumed to be a function of the difference between the local temperature and the arterial blood temperature. In previous works a linear function has been considered. This linear model, however, disregards the local thermoregulating influence of the blood flow. In this work the thermoregulation has been taken into account by assuming the blood flow cooling effect to be a non-linear function of the difference between local and arterial blood temperature. The effect of a cooling fluid forced past the surface of the living tissue has also been taken into account. The theoretical temperature distribution induced by exposure to electromagnetic fields has been determined according to the following steps: at first the non-linear operator has been linearized by using the iterative Newton-Raphson's method; then a matrix formulation has been obtained through the moment method. In particular, the case of a slab simulating living tissues, which is irradiated by a plane electromagnetic wave, has been considered. The temperature distribution has been carried out for various types of non-linear blood cooling functions, in order to evaluate the matching between the assumed mathematical model and the true biological phenomena.

0549 RADIOTHERAPY-HYPERTHERMIA ASSOCIATION: TWO PATIENTS (MEETING ABSTRACT). (Eng.) Belli-ossi, A. (Centre Eugène Marquis 35000 Rennes, France); Flaury, F.; de la Perelle, A.; Kernec, H. Strahlentherapie 158(6):379; 1982.

Many authors have reported that radiotherapy-hyperthermia association potentializes the effect of each method. We present two patients who confirm the favorable effect of this association. Hyperthermia was delivered by a 13.56 MHz generator (STAE prototype) used in capacitive diathermy. Two 1-hr sessions took place a week, every 2 or 3 days, 3 hr after radiotherapy. The first patient was treated for cutaneous recurrence of a cancer of the right pyriform sinus. In December 1980, electrontherapy was administered, associated twice a wk with hyperthermia. The result was positive but, in May 1981, two permeation nodules appeared out of the treated lesion. For 7 wk these nodules were treated each week by three electrontherapy sessions (3 Gy) and two hyperthermia sessions (1 W.cm^{-2}). In July, the lesions had disappeared; in December, the results were excellent. The second patient was bed-ridden by the recurrence of a prostatic cancer, which had been operated on, then treated by

cobaltotherapy (60 Gy) 7 yr ago. Cobaltotherapy (2.2 Gy a session) and hyperthermia (0.5 W.cm^{-2}) twice a wk had been given for 5 wk. The results were excellent. The patient died of a myocardial infarction 1 yr later.

0550 CLINICAL PRACTICE OF 434 MHZ MICROWAVE HYPEROTHERMIA (MEETING ABSTRACT). (Eng.) Bey, P. (Centre Alexis Vautrin, Avenue de Bourgogne, 54511 Vandoeuvre les Nancy, France); Marchal, C.; Hoffstetter, S.; Metz, R.; Escanye, J. M.; Robert, J. Strahlentherapie 158(6):379; 1982.

To determine the efficacy of hyperthermia alone or combined with radiotherapy, we compared the regressions of heated tumors with unheated others in each patient. Thirty-eight patients with advanced cancer, mainly local evolutions of ear-nose-throat carcinomas, melanomas or skin metastasis, have been treated using a 434 MHz microwave hyperthermia apparatus. Microthermo-couples are placed inside or underneath the tumors and temperature is controlled by a computer which automatically shuts off the power for thermometry and regulates tumor thermal level between 41 and 45 °C. Forty-five tumors were submitted to microwave-induced hyperthermia (5 sessions of 45 min, 5 D/7 or 3 D/7). Radiotherapy followed hyperthermia with a time interval ranging from 3 to 30 min. Different total radiation doses from 12 to 30 Gy were delivered every day or thrice a wk. For 6 patients, hyperthermia was associated with conventional chemotherapy. Tumor response was assessed by measuring the tumor volume. Hyperthermia combined with radiotherapy sessions seems the most effective for inducing tumor regressions (>50% cases). This 434 MHz microwave hyperthermia apparatus is well adapted for recurrent lymph nodes of head and neck, even those pretreated with a high radiation dose.

0551 2450 MHZ HYPERHERMIA MONITORING SYSTEM; CLINICAL APPLICATIONS FOR THE TREATMENT OF SUPERFICIAL TUMORS (MEETING ABSTRACT). (Eng.) Bordure, G. (Centre d'Etudes d'Electronique des Solides, Univ. Sciences et Techniques du Languedoc, 34060 Montpellier Cedex, France); Delauzun, J. P.; Richard, J. P.; Dubois, J. B.; Hay, M. H. Strahlentherapie 158(6):379; 1982.

Our study deals with a hyperthermia system which employs open space applicators and computer monitoring for the treatment of superficial or nearly superficial tumors. The applicator consists of a rectangular wave guide coupled with a cooling system for superficial tissue which introduces air along the guide axis. Following an established protocol, this applicator rapidly creates a homogeneous temperature distribution (between +2 and +3 °C) up to to a depth of 3 cm and covering a surface of 16 cm² comparable to the

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results obtained with microwaves at 434 MHz using a direct contact waveguide and tissue cooling system). Hyperthermia was monitored by a single temperature sensor implanted in the superficial tissue. A micro-program regulates microwave power and reduction of superficial temperature. The program was designed to reach a predetermined temperature with minimal delay and without overheating of superficial tissue. The technique is well tolerated by the patient and is without risk to either operator or patient. Our results were based on our experience with 10 patients with recurrent thoracic wall tumor from breast carcinomas. Consideration is given to the potential use of open space applicators to treat surfaces on the order of 100 cm² by a system which can be perfectly adapted to numerous clinical situations.

0552 A STUDY OF RF 27 MHz ELECTROMAGNETIC FIELD TECHNIQUES FOR THE LOCALIZED HEATING OF HEAD AND NECK TUMORS (MEETING ABSTRACT). (Eng.) Carnochian, P. (Royal Marsden Hosp., Fulham Road, London SW 3, England); Jones, C. H. Strahlentherapie 158(6): 379; 1982.

The effective use of localized hyperthermia in cancer treatment requires careful optimization of the heating techniques employed. To this end useful information may be obtained about the design of applicators by investigating the distribution of power deposited within phantoms *in vitro*, and by the assessment of applicator performance *in vivo* using invasive thermometry and/or thermography. Infrared thermography has been utilized to investigate the heating patterns produced by both capacitive and inductive short-wave diathermy applicators in phantoms having the electrical characteristics of typical tissues. The boundaries within the layered, cylindrical phantoms were chosen to approximate to some of the major dielectric discontinuities of the cervical region. The results of these studies indicate the potential of the capacitive diathermy technique for heating small volumes of subcutaneous tissue. Further studies of excised animal tissue using this technique, have suggested that anomalous heating of tissues in the region of the cervical vertebrae is unlikely. *In vitro* studies allow investigation of only those parameters which have an influence upon the distribution of power absorbed by tissues from the electromagnetic field, and knowledge of the thermal properties of tissues *in vivo* is necessary before localized hyperthermia treatment can be optimized. A method is described whereby the careful positioning of implanted thermocouple probes used in conjunction with external heat sources allows: a) the optimization of parameters influencing thermal distributions *in vivo*, b) an estimation of the thermal dose delivered to a tumor during heating, and c) a quantitative index of the blood cooling efficiency of peripheral tumor regions.

0553 FOCUSED MICROWAVE HYPERHERMIA AT 1-3.5 MHZ (MEETING ABSTRACT). (Eng.) Conway, J. (Sheffield Univ. and Area Health Authority, Dept. Medical Physics and Clinical Engineering, Royal Hallamshire Hosp., Glossop Road, Sheffield S10 2 SF; England); Melek, M.; Anderson, A. P.; Brown, B. H. Strahlentherapie 158(6):380; 1982.

A technique to introduce hyperthermia at depth within the human body using focussed microwave arrays has been studied. A computer simulation of the power dissipation within a cylindrical body, assuming uniform permittivity and attenuation, indicates that, by using a semi-circular or semi-elliptic geometry of radiators and applying appropriate phase and amplitude illumination, a significant thermal enhancement may be induced at a site within the body compared with its surroundings. A configuration of 11 array elements (6 elements curved around the cylinder and 5 elements along the cylinder axis) yields a sufficient energy concentration to produce a focussed region heated twice as much as any other region inside the cross-section. Computer simulations indicate that the size, shape, and position of the high temperature region should be approximately controllable and that the stability of the system is tolerant to typically 20% errors in the phases and amplitudes of the radiators. Measurements have been performed on a simple thorax phantom using the same arrangement of dipole elements described above. The elliptical body was filled with water-saturated sand yielding a permittivity of 22 and an attenuation constant of 140 dB/m. An antenna probe was utilized to measure the intensity distribution at 49 points within the body. Results indicate a high intensity peak at a region 5 cm deep into the thorax phantom, the second high intensity region being 40% below and occurring at 1 cm deep. These results agree well with theoretical computer predictions. In practice, the focussing effect may be modified by thermal dissipation due to blood flow and heterogeneity of the body. However, the relative magnitude of the focussed region could be enhanced by air cooling of the skin surface. Results obtained so far indicate that heating of deep seated tumors within the body is possible using a non-contacting focused microwave array system.

0554 EXPERIENCE WITH 10-35 MHz RF IN CLINICAL HYPERHERMIA (MEETING ABSTRACT). (Eng.) Griffiths, H. (Physics Dept., Velindre Hosp., Whitchurch, Cardiff, England). Strahlentherapie 158(6): 382; 1982.

A series of selected patients with advanced cancer have been treated by hyperthermia using a LeVeen RF Thermotherapy machine. This machine uses capacitive coupling to apply the radiofrequency (RF) power to the tissue. Saline-filled pillows were placed between the RF electrodes and the skin to enhance coupling. Cooled saline was circulated through the pillows during treatment to avoid excessive heating

of the superficial tissue. Tumor temperatures between 43°C and 45°C were taken as the objective of each treatment, temperature profiles in the tissue being measured with copper-constant thermocouples. Patient response was assessed using a number of different criteria.

0555 THE INFLUENCE OF WHOLE-BODY HYPERTERMIA ON SIDE-EFFECTS OF DOXORUBICINE AND RADIOTHERAPY I. ATS (MEETING ABSTRACT). (Eng.) Hinkelbein, W. (Zentrum Radiologie, Abteilung Strahlentherapie, Univ. Freiburg i. Br., W. Germany); Engelhardt, R.; Behlert, W.; Neumann, H.; Wannenmacher, M. Strahlentherapie 158(6):382; 1982.

The effects of two combined treatment modalities (simultaneous combination of whole-body hyperthermia and doxorubicine treatment, simultaneous combination of whole-body hyperthermia and total-body irradiation) were studied in rats. Whole-body hyperthermia was induced by UHF (41°C±0.35°C core temperature for 10 and 20 min). Doxorubicine was administered in two injections (5 mg/kg on day 0 and 8 mg/kg on day 14). Total-body irradiation was 3.5 Gy γ -rays (Co60). Haematotoxic (myelotoxic) and cardiotoxic side-effects were investigated. Hyperthermia alone produced leucocytosis and isolated sarcolysis. In combined treated rats intensified and reduced side-effects of doxorubicine and irradiation were seen depending on heating time.

0556 ASSESSMENT OF THERMOCOUPLE PROBES FOR USE IN RF FIELDS (MEETING ABSTRACT). (Eng.) Joiner, M. C. (Gray Laboratory of the Cancer Res. Campaign, Mount Vernon Hosp., Northwood, Middlesex HA6 2RN, England); Bremner, J.; Vojnovic, B. Strahlentherapie 158(6):384; 1982.

In order to compare different heating methods and quantify temperature patterns during hyperthermia, measuring probes should be able to accurately resolve temperature gradients in heated tissues. Such gradients can be large ($>1\text{ }^{\circ}\text{C/mm}$) in small experimental animal tumors heated by RF, microwaves or ultrasound where heated volumes are typically less than 0.5 cm^3 . Data will be presented showing the extent to which bare (exposed junction) or metal and plastic sheathed thermocouple probes of varying sizes "smooth out" a sharp temperature change across a thin membrane. For probes sheathed in hypodermic needles, this effect is due to heat conduction along the metal shaft from hot to cooler regions and increases as needle diameter increases. Probes sheathed in plastic may read incorrectly if the connecting wires are large and the surrounding plastic tube has low thermal conductivity. The use of RF for heating generally leads to non-thermal interference with electronic temperature measuring equipment which necessitates the heating field

being turned off before a measurement is made. However, the use of metallic probes in direct electrical contact with surrounding tissue also results in an apparent temperature rise in the immediate vicinity of the probe which must be allowed to decay after the RF has been switched off before an accurate measurement of the true temperature in the tissue bulk can be made. This effect is not seen with electrically insulated probes which are therefore preferable for use in RF fields.

0557 EXPERIMENTAL AND CLINICAL STUDIES OF VARIOUS SYSTEMS OF ELECTROMAGNETIC HYPERTERMIA (0.5 MHz, 13 MHz, 434 MHz, 2450 MHz) (MEETING ABSTRACT). (Eng.) Lauche, H.-M. (Lab. Thermologie Biomedicale, Faculte de Medecine, Univ. Louis Pasteur, 11, rue Humann, 67085 Strasbourg Cedex, France); Guerquin-Kern, J. L.; Pillement, P.; Moyses, B.; Gautherie, M.; Mechlin, G. Strahlentherapie 158(6):385; 1982.

The proper use of electromagnetic hyperthermia for cancer treatment requires comprehensive knowledge of numerous parameters concerning the target volume and the irradiation system (generators and applicators). Before starting investigations on patients, experimental studies of several pieces of equipment were effected using two different physical models: 1) excised animal tissues and post operative specimens, e.g. after mastectomy (analysis of deep temperature with an infrared thermograph, immediately after the irradiation); 2) on original phantoms made of transparent gels with known electric, dielectric and thermal properties corresponding to those of biological tissues (analysis of deep temperature by means of thermosensitive liquid crystal film) during the irradiation. Additional studies were carried out in animals, in particular dogs, *in vivo* after anesthesia and then post mortem, in order to investigate the influence of blood flow and regulatory processes. For these experiments, deep temperature was controlled using implanted needle probes, either metallic or non interfering. Two categories of methods were used; a) capacitive hyperthermia using generators operating in the radiofrequency range (0.5 MHz, 13 MHz) with external flexible applicators, or implantable needle probes allowing accurate heating *in situ*; b) radiative hyperthermia using generators operating in the microwave range (434 MHz, 2450 MHz) with new systems of external applicators (surface cooling, cross-fire arrangement, ...). From these studies it follows that (1) models may only be used to design, improve and compare heating systems, and (2) the tumor temperature pattern is largely dependent upon blood flow, histology and morphology of host and tumor. Protocols of therapeutic trials may therefore be established on phase I studies on patients in order to take the individual changes of vascular and thermal conditions into account. To this purpose, preliminary investigations have been effected on patients with advanced cancer, mainly skin metastases and breast carcinomas for which temperature control and clinical follow-up is relatively easy.

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Emphasis was laid on combination of hyperthermia with radiotherapy.

0558 LOCAL MICROWAVE HYPERHERMIA COMBINED WITH RADIOTHERAPY: ONE YEAR'S EXPERIENCE (MEETING ABSTRACT). (Eng.) Valdagni, R. (Oncologic Center, Istituti Ospedalieri S. Chiara, 38100 Trento, Italy); Amichetti, M. Strahlentherapie 158(6):390; 1982.

From February 1981 to February 1982, 26 patients (32 fields) with histologically proven malignancy were treated with hyperthermia combined with radiotherapy. Most of the patients had failed conventional treatments. The patients were 19 male and 7 female, and the median age was 62 years, ranging from 45 to 94. Of the 26 patients, 25 had Karnofsky indices greater than 50%. Histologically the lesions include: 17 squamous carcinoma, 8 malignant melanoma, 3 adenocarcinoma, and 4 chordoma. RT (2-3-5 fractions/wk - dose per fraction: 1.80-6.00 Gy T. D.: 8.00-65.00 Gy) was applied using 2 linear accelerators (Mevatron Siemens) at 6-12 MV (electron or photon beam). Simultaneous microwave H (209 heat treatment sessions), external or interstitial, (42.5-44.0 C x 20 to 55 min 2-3 fractions/wk) was delivered by BSD - 1000 unit. Thermometry was performed by means of non-perturbing probes placed on the skin and in catheters inserted in the tumors. The frequency (300-900 MHz) and power (up to 130 W) used depended on the depth and size of treated lesions (maximum diameter: 8 cm, up to 5 cm depth). An analysis of technical data and clinical results will be presented.

0559 PRELIMINARY CLINICAL RESULTS OF LOCAL HYPERHERMIA IN COMBINATION WITH LOW DOSE RADIOTHERAPY (MEETING ABSTRACT). (Eng.) van der Zee, J. (Dept. Exp. Radiotherapy, Erasmus Univ. Rotterdam, Rotterdamsch Radiotherapeutisch Instituut, The Netherlands); van Rhoon, G. C.; Wike-Hooley, J. L.; Reinhold, H. S. Strahlentherapie 158(6):390-391; 1982.

In the Rotterdam Radiotherapeutic Institute, 80 patients have been treated with local hyperthermia. This communication reports on the results from 28 of these patients, treated on 34 fields with local hyperthermia combined with a low dose of radiotherapy, and having evaluable tumor responses. Lesions treated were predominantly recurrences in previously irradiated fields. Histologies included mammary, lung, gynecological, kidney, and skin carcinoma. Tumors were heated using electromagnetic radiation with frequencies of 1450, 433 or 27 MHz. Temperatures were always measured with thermocouple needles and more recently also with an optical fiber temperature measuring system. Local hyperthermia was administered twice weekly, 30-60 min following radiotherapy, for a

mean treatment duration of 60 min (3-10 treatments). The average radiotherapy dose was 20 ± 3.4 Gy. As the "hyperthermia dose" we selected the mean of maximum temperatures of all points measured in all treatment sessions, the average for all patients being 41.6 ± 1.4 C (range 40.5-45.3 C). Tumor response was defined following WHO criteria (complete response = disappearance of tumor; partial response = 50% or more decrease in tumor size). In this heterogeneous, non-randomized group of patients we found a response rate of 80%; complete response in 6/35 fields and partial response in 22/35 fields. The separate contributions of both treatment modalities to response were investigated retrospectively. We found no significant correlation between either the total X-ray dose or the X-ray fraction size and response rate, but the response rate (CR + PR) was found to be correlated with the mean of all maximum tumor temperatures. This indicates that an increasing temperature results in an increasing response rate. The combined therapy, in this heterogeneous group of patients, resulted in a 50% response rate at a mean maximum tumor temperature of 41.0 C and an 80% response rate at a mean maximum temperature of 42.3 C.

0560 INTERFERENCE OF 433 MHZ MICROWAVES WITH A MEGAVOLTAGE LINEAR ACCELERATOR (MEETING ABSTRACT). (Eng.) van Rhoon, G. C. (Dept. Experimental Radiotherapy, Erasmus Univ., Rotterdam, The Netherlands); van der Poel, J. A. Strahlentherapie 158 (6):391; 1982 (1 ref).

A series of experiments was conducted to investigate the effect of 433 MHz microwaves on the performance of a megavoltage linear accelerator, the Sagittaire. The microwave equipment consisted of a Siretherm 509 Siemens generator, power 250 W and a standard circular field dipole antenna. In all experiments the microwave unit stood in a room adjacent to that of the accelerator. Microwave power levels were measured with a Narda broadband radiation monitor, model 8300, and at levels greater than 200 mW/cm^2 at 5 cm from the antenna no more than 2 mW/cm^2 were ever detected in the control room of the Sagittaire. The elements of the Sagittaire itself were contained in 4 separate rooms, i.e., for the accelerator tube, the control units and the treatment of the patients. Measurements of the accelerator performance were achieved with the use of conductor and thermoluminescence (TLD; lithium-fluoride) dosimetry systems. For the TLD measurements the rods were situated in a $18 \times 28 \times 25 \text{ cm}^3$ water filled perspex box. In accordance with earlier findings by W. J. Kopecky et al., we also found that the normal operation of the Sagittaire was disturbed. However, our observations do not indicate that there is a change in the dose delivered, but only showed that the microwave interference was directed towards the beam energy. For example, a consol set beam energy of 25 MeV increased to 29 MeV when the microwave generator operated freely at maximum power. When part of the microwave energy was absorbed by a 10 cm thick muscle phantom in front of the antenna there was

still an increase of the beam energy to 26.9 MeV. With the measurements performed, no interaction of microwaves with beam homogeneity could be demonstrated. If the dose measured at the dose maximum in the water phantom was corrected for the change in energy, there was no evidence that the delivered dose was different from the one set on the control console. Interference between these two systems is very difficult to discern. We would therefore like to advise, in agreement with the earlier investigators, that each accelerator/hyperthermia installation be carefully checked for possible interference effects, even when the accelerator appears to be operating normally.

0561 BLOOD FLOW AND OXYGEN SUPPLY TO MALIGNANT TUMORS DURING HYPERTERMIA-EFFECT OF VARIOUS DOSES (MEETING ABSTRACT). (Eng.) Waupel, P. (Dept. Physiology, Univ. Mainz, D-6500 Mainz, W. Germany); Otte, J.; Muller-Klieser, W.; Manz, R. Strahlentherapie 158(6):391; 1982 (1 ref).

Since tumor tissue oxygenation seems to play a decisive role during heat treatment *in vivo*, systematic investigations concerning the respiration rate of isolated ascites tumor cells, the O₂ consumption of solid tumors *in situ*, and both the oxygen partial pressure distribution and the oxyhaemoglobin saturation (HbO₂) of single red blood cells in tumor microvessels have been performed during and immediately after elevated tissue temperatures. The results clearly show that changes in tumor oxygen supply during hyperthermia are predominantly mediated through changes in tumor blood flow which showed the same directional changes. The present series of experiments was performed in order to get some data on the susceptibility of tumor oxygenation to various thermal doses as determined by the duration of heating and the tissue temperature increment during treatment. As a measure of tissue oxygenation, the oxyhaemoglobin saturation of single erythrocytes within tumor microvessels was determined immediately after localized microwave hyperthermia (2.45 GHz). For the present work, tumors of DS-carcinosarcoma implanted in the hind foot dorsum of SD-rats were used. The experiments were performed on 70 tumors with a mean wet wt of 3 g. Mean tissue temperatures were held at four levels: control (34 C), 40 C, 43 C and 45 C for 30 and 60 min. The results obtained indicate that thermal doses below 260 C/min can evoke an improvement of the tissue oxygenation. At higher doses a deterioration of the oxygenation status occurred. A 50% reduction of the tissue oxygenation was found at a thermal dose of approximately 400 C/min. The present study provides evidence that tissue oxygenation during heat treatment is probably dependent on the thermal dose. This is in contrast to previous findings of Reinhold and Van den Berg-Blok who found comparable effects of hyperthermia on microcirculation at different thermal doses. Further investigations will be necessary to clarify these controversies.

0562 DEVICE FOR TEMPERATURE MEASUREMENT USING LIQUID-CRYSTAL PROBES DURING HIGH-ENERGY SHORTWAVE HYPERTERMIA (MEETING ABSTRACT). (Eng.) von Ardenne, M. (Res. Inst. Manfred von Ardenne, DDR-8051 Dresden, W. Germany); Bohme, G.; Kell, E.; Schlechte, P. Strahlentherapie 158(6):391; 1982.

Certain liquid-crystal mixtures are known to exhibit color changes over a limited and adjustable operating temperature range. These color changes correspond to shifts of intensity, shape of the maximum, and wavelength of the reflected light. Known devices measuring mainly intensity of reflected light are affected by several artefacts, e.g., variable sensitivity of the optoelectronic detector, instability of the light source and its variation with the ambient temperature. We present a measuring device, which exclusively detects and evaluates the temperature-dependent wavelength of the maximum of the light reflected by the liquid crystals and which is insensitive to external influences exemplified above. A minute amount of liquid-crystal mixture is entrapped into a sufficiently small probe which is introduced into the tumor to be heated or into healthy reference tissue, respectively. The probe is connected with the detector unit by means of a two-component fibre optic. At the site of high-energy electromagnetic fields there is hence only the probe, which is indifferent to these fields and vice versa, whereas the electronic setup is placed in a shielded room apart from the patient. The recording unit contains an automatically and periodically tuned monochromator with chopped light-source and an electronic part consisting of the optoelectronic detector, the noise-limiting amplifier and the data-processing unit. The apparatus delivers values representing temperature. Each value persists on the display during measuring cycle of the next value. The temperatures measured are also available as analogue signals at the output for recording. The prototype described has been successfully tested during clinical trials using the CMT Selectotherm technique for heating human tumors at 27.12 MHz.

0563 UPTAKE OF ^{99m}Tc-MDP AT A FRACTURE SITE TREATED WITH ELECTROMAGNETIC INDUCTION OF CURRENT (MEETING ABSTRACT). (Eng.) McCarthy, I. D. (Univ. Dept. Orthopaedic Surgery, Princess Margaret Rose Orthopaedic Hosp., Fairmilehead, Edinburgh, Scotland); Annan, I. H.; Loudon, I.; Law, H. T.; Hughes, S. P. F. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 10-12 September 1982 in Oxford, England; 1:1; 1982.

The uptake of the bone seeking tracer, ^{99m}Technetium-labelled methylene diphosphonate (^{99m}Tc-MDP), was quantitatively measured to objectively assess the effectiveness of induced electrical current in enhancing fracture healing. A fracture model was produced by open osteotomy of the sheep tibia. Two Helmholtz coils which were driven by a trapezoidal

wave form in which the rising and falling slopes were approximately equal were placed on either side of the treatment site. At weekly intervals, for 5 wk after the osteotomy, ^{99m}Tc -MDP was injected into the sheep. The count rate at the fracture site was measured at 1, 5, 15 and 60 min after the injection by placing a collimated scintillation detector on the plates over the fracture site. In eight sheep studied (4 experimental and 4 controls), the count rate at 60 min increased during the 5 wk studied (360 ± 90 to 760 ± 280 for the experimental group, and 230 ± 40 to 670 ± 200 for the controls). At each of the measurement times, the values in the experimental animals were relatively higher than in the control sheep, e.g., 0.40 ± 0.09 compared with 0.26 ± 0.04 at 1 min after injection (where the data had been normalized to unity at 0 min after injection). This difference was statistically significant ($p < 0.05$). The results demonstrate that *in vivo* measurements can detect changes in fresh fractures stimulated with induced electrical currents.

0564 EFFECTS OF ELECTRICAL STIMULATION ON CALCIUM-45 UPTAKE IN FRACTURED FIBULAE FROM NORMAL AND THYROPARATHYROIDECTOMIZED RABBITS (MEETING ABSTRACT). (Eng.) Guy, D. K. (Dept. Anatomy, Health Sciences Center, Univ. Louisville, Sch. Medicine, Louisville, KY, 40292); Wald, H. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:2; 1982.

An investigation was undertaken to determine whether electrical stimulation of fracture healing enhances the uptake of calcium into bone and whether the enhanced mineralization, if present, is independent of hormonal influence. A transverse, mid-shaft fracture of the fibula was produced bilaterally in 20 New Zealand White rabbits. The right fibula of each animal was electrically stimulated with 18-20 μA of direct current while the left side served as control. Ten of the rabbits also underwent thyroparathyroidectomy at the beginning of the experimental period. These ten animals received thyroid hormone as replacement therapy but were considered to have an absolute deficiency of calcitonin and parathyroid hormone. All animals received ^{45}Ca iv at intervals during the healing period. At the end of the 21-day study, bone samples from both fibulae and the proximal half of the radius were taken from each animal. The amount of ^{45}Ca per unit wt of bone was determined by analyzing the samples on a liquid scintillation counter. The results demonstrated no difference in ^{45}Ca uptake between stimulated and non-stimulated fibulae. Fractured bones did exhibit a significant increase in uptake over non-fractured bones. In the absence of calcitonin and parathyroid hormone, all bone categories studied demonstrated a statistically significant increase in ^{45}Ca uptake. Since all bone categories were equally affected, these data are believed to reflect an increase in the turnover rate rather than an actual increase in

the total amount of calcium present.

0565 ELECTRICAL ACCELERATION OF THE RATE OF FRACTURE HEALING IN THE PRIMATE METATARSAL (MEETING ABSTRACT). (Eng.) Walter, J. (Pennsylvania Coll. Podiatric Medicine, 8th at Race St., Philadelphia, PA 19107); Harrington, D.; Walker, T.; Chen, T.; Black, D.; Bodamer, W. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:3; 1982.

The primate *Cebus Albafrons* (organ grinder monkey) was used to explore the effects of small amounts of electric current on acceleration of fracture healing in the primate metatarsal. Young (late adolescent) monkeys were chosen because of the biological and biomechanical similarities between the primate and the human. Each animal was anesthetized and the dorsal region of the third metatarsal was exposed on each foot. Two Kirshner wires were inserted proximally and distally, perpendicular to the long axis of the bone, in the dorsal aspect of the metatarsal. Then a third Kirshner wire was placed and fixed horizontally across both vertical wires, thereby creating an external fixation device. Next, a 2.0-mm osteotomy was made between the proximal and distal fixation pins, and a stainless steel electrode (teflon coated except for the tip) was placed in the osteotomy site and fixed in place by being attached to the horizontal portions of the external fixation device. The incisions were closed and casted, then one foot was chosen at random to be the experimental side (active electrode) while the other metatarsal served as control (dummy electrode). Anodes were placed in different sites. Three groups of animals with 14 animals per group were used for this study. Group A represented 3 days post-operative, Group B was 15 days post-operative and Group C ran for 22 days after surgery. The data indicated that the electrically stimulated osteotomies healed faster than the control groups, that the electrically stimulated bone appeared as normal, woven bone with little or no endochondral formation, and its ossification was more advanced than control samples. Osteoblastic activity and vascularization was also greater in experimental samples.

0566 BIOELECTRIC AND HISTOMORPHOMETRIC CHANGES DURING FRACTURE HEALING (MEETING ABSTRACT). (Eng.) Chakkalakai, D. A. (Orthopaedic Res. Lab., VA Medical Center and Dept. Orthopaedic Surgery, Univ. Nebraska Medical Center, Omaha, NE 68105); Lippiello, L.; Connolly, J. F. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:4; 1982.

The correlation between local electric fields calculated from voltage measurements in bone and new bone formation obtained in the osteotomized canine radius was investigated. Four Ag/AgCl bead electrodes were implanted in the bone; two in the cortical region and two in the medullary region. Voltage measurements were done 1x wk. At 2, 3, 10 and 12 wk post osteotomy the dogs were sacrificed; the radius was sectioned transversely into 2-mm sections and a point counting method was used to quantitate new bone formation. From the voltage measurements the average electric field strengths in the regions between electrodes were calculated. A correlation was found between the combination of magnitude and duration of electric field of negative polarity ("field dose") and the amount of new bone formation. In one dog the amounts of new bone in the regions proximal and distal to the osteotomy were comparable corresponding to similarity of the "doses" in the two regions. In contrast, in a second dog, considerably more bone formation occurred in the distal region corresponding to the much larger "dose" there compared to the proximal region. Work is in progress to seek further correlations between osteogenesis in specific stages and the details of changes in the local electric field.

1567 PRIMARY INDUCED CELLULAR CHANGES AND CELL SPECIFICITY IN PULSED CAPACITIVE STIMULATION OF BONE CELLS IN VITRO (MEETING ABSTRACT). (Eng.) Korenstein, R. (Weizmann Inst., Dept. Membrane Res., Rehovot, Israel); Somjen, D.; Fischler, H.; Binderman, I. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:5; 1982.

Results of a study on pulsed capacitive stimulation of mixed population of bone cells in culture are reported. Stimulation of bone cells was performed by a series of rectangular voltage pulses (25 usec width, 3 Hz repetition rate) of varying amplitudes, lasting 5 min. Low field strength stimulation (13 V/cm prevailing in the culture medium) caused immediate decrease of 30% in intracellular level of cyclic AMP (cAMP) which was followed by a 1.3- to 1.4-fold increase in DNA synthesis 24 hr later. Middle field strength (22 V/cm) caused no change both in cAMP and DNA. High field strength (54 V/cm) caused a 1.8-fold increase in cAMP level and a 2.5-fold increase in DNA synthesis. These bone cell cultures, prepared from rat embryocalvaria were shown to respond both to parathyroid hormone (PTH) and to prostaglandin-E₂ (PGE₂). When bone cells were subcultured they lost their responsiveness to either PTH or electric field but responded to PGE₂ by an increase in cAMP production. Furthermore the subcultures lost their responsiveness to either PTH or PGE₂ in terms of DNA synthesis and maintained their responsiveness to low electric fields only (1.3-fold increase in DNA synthesis). It is suggested that the cells that respond to low field stimulation are the PGE₂ sens-

sitive cells and those that respond to high fields are the osteoclast-like, PTH-responding cells. Thus different cell types are stimulated at different regions of the applied electric fields. The electrical stimulation was shown to induce cascade of biochemical events, where the immediate biochemical changes included cyclic nucleotide changes (cAMP) and ion fluxes (Ca²⁺ fluxes). This transmission of the electric stimulus at the membrane level through a second messenger mechanism is compared to the stimulus-signal transmission mechanisms by hormones and growth factors.

0568 ALTERNATING MAGNETIC FIELDS ENHANCE DNA SYNTHESIS IN FIBROBLASTIC CELLS (MEETING ABSTRACT). (Eng.) Liboff, A. R. (Dental Res. Branch, Stop #18, Naval Medical Res. Inst., Bethesda, MD 20814); Strong, D. M.; Wistar, R. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:6; 1982.

The effect of sinusoidally varying magnetic fields on DNA synthesis in cells was investigated *in vitro*. A pair of matched incubators equally fitted with a specially designed set of coils, 0.5-m inside diameter and 0.25-m in length. Three-coil configurations were employed with spacing equal to half the radius, N turns on the center coil and 2N on the end coils, in order to optimize the field uniformity over a larger volume than could be obtained with a classical Helmholtz arrangement. Two independent series of experiments were performed using this set-up. Human foreskin fibroblasts (HEM-HFS-15) were seeded into 24- and 96-well tissue culture plates using DMEM and 10% FCS and the plates distributed equally between the experimental and control incubators. An amplitude of 0.2 G was used as well as frequencies ranging between 40 and 80 Hz. The relative amounts of thymidine uptake in the experimental and control plates were determined using: (1) a 1-hr ³H-thymidine pulse, (2) an 18-hr pulse, and (3) an integrated ³H-thymidine label introduced with the initial inoculation. It was found that in 45/48 paired plates, the level of incorporated thymidine was significantly higher in the experimental plates; it was further observed that the amount of incorporated thymidine in exposed cells peaked at a two-fold ratio over the control cells in the vicinity of 20 hr after the beginning of exposure. It is concluded that there is a consistent stimulatory effect of sinusoidal magnetic fields on the DNA synthesis of human foreskin fibroblasts *in vitro* and that the specific pulsed electromagnetic field waveshape is not required to elicit this effect.

0569 THE EFFECT OF PULSATING ELECTROMAGNETIC FIELDS ON PROSTAGLANDIN SYNTHESIS IN OSTEOBLAST-LIKE CELLS (MEETING ABSTRACT). (Eng.)

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Johnson, D. E. (Dept. Oral Biology, Univ. Connecticut, Sch. Dental Medicine, Farmington, CT 06032); Rodan, G. A. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982, in Oxford, England; 2:7; 1982.

The effect of pulsating electromagnetic fields (PEMF) on prostaglandin synthesis was investigated in the rat osteosarcoma-derived osteoblastic cell line ROS 17/2.8. Cells were grown to confluence in F-12 medium supplemented with 10% fetal bovine serum and were exposed to PEMF for up to 24 hr. Prostaglandin E was measured in cell media by radioimmunoassay; the release of ¹⁴C-arachidonate (the prostaglandin precursor) from phospholipids of prelabelled cells and its conversion to ¹⁴C-PGE₂ were assessed by thin layer chromatography of organic solvent media extracts; the activity of cyclooxygenase, the prostaglandin synthesizing enzyme, was assayed by incubating living cells with arachidonate and measuring PGE by RIA. It was found that PEMF: (i) had no effect on cyclooxygenase activity, which had a K_m of 20 μ M and a V_{max} of 160 ng/10⁶ cells/min; (ii) stimulated the release of arachidonate from phospholipids by about 50%; and (iii) increased PGE production from 200 pg/hr/culture to 350 pg/hr/culture. The PGE concentration in culture media exceeded 10 nM, a level which enhances cyclic AMP accumulation, growth and osteoclast activation in bone explants. The stimulation of PGE synthesis by PEMF in osteoblastic-lineage cells is consistent with membrane-mediation and cyclic AMP-involvement in the transduction of electrical signals and the subsequent effects on growth and maturation.

0570 IN VITRO CAPACITIVELY COUPLED ELECTRICAL STIMULATION OF BOVINE ARTICULAR CHONDROCYTE PELLETS IN VARYING SERUM CONCENTRATIONS (MEETING ABSTRACT). (Eng.) Brighton, C. T. (Dept. Orthopaedic Surgery, Univ. Pennsylvania, Philadelphia, Pa 19104); Unger, A. S.; Stambough, J. L. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982, in Oxford, England; 2:8; 1982 (2 refs).

A facilitory response of *in vitro* bovine articular chondrocyte pellets is reported which is dependent on the concentration of newborn calf serum (NBCS) in the presence of a capacitively coupled field. Articular cartilage was obtained in a sterile manner from the stifle joints of male Holstein calves (1-2 wk old). Pellets were formed from 4 x 10⁶ isolated articular chondrocytes prepared by selective matrix digestion using sequential enzymes (trypsin, hyaluronidase, collagenase) and grown in tissue culture media (TCM) with 10% NBCS for 72 hr prior to stimulation. Tissue culture media with 1% or 10% NBCS was labelled with ³⁵S-sulphate (10 μ Ci/ml) or ³H-thymidine (5 μ Ci/ml). The freshly labelled system was stimulated for 24 hr in an externally applied 150-V peak-peak, 50

KHz, sine wave capacitively coupled field which gave a current density in each 18.1 cm² petri dish of 57 μ A/cm² (RMS value). In the presence of a current density of 37 μ A/cm²/dish (250 V peak-peak) and TCM with 10% NBCS, ³H-thymidine incorporation per μ g protein and DNA was significantly increased ($p < .01$), but ³⁵S-sulphate incorporation per μ g protein was significantly decreased ($p < .05$). Repeating the same experiment in 1% NBCS showed an increase in ³⁵S-sulphate incorporation per μ g protein and DNA ($p < .01$), but ³H-thymidine incorporation was not significantly affected. A current density of 37 μ A/cm²/dish (150 V peak-peak external signal) further enhances these *in vitro* effects in a statistically significant manner. These findings emphasize the importance of serum concentration in *in vitro* cellular systems. More importantly, this study shows that a capacitively coupled electric signal can act to modulate a predetermined cellular response in mammalian articular chondrocytes.

0571 STIMULATION OF CONNECTIVE TISSUE PROTEIN SYNTHESIS IN FIBROBLAST CULTURES BY PULSED MAGNETIC FIELDS (MEETING ABSTRACT). (Eng.) Murray, C. (Strangeways Res. Lab., Cambridge, England). In: Transactions of the Second Annual Meeting of the Biological Repair and Growth Society, held on 20-22 September 1982, in Oxford, England; 2:9; 1982.

The effect of the Bi-Osteogen system (E.B.I., U.K., Ltd) on protein synthesis, in particular the synthesis of matrix components, by embryonic chicken tendon fibroblasts (CETF) in culture was investigated. Primary cultures of CETF were exposed to pulsed electromagnetic fields (PMF) of the repetitive pulse burst type on a 6 hr-on/6 hr-off cycle through a 9-day growth period. Cell numbers were measured electronically and protein synthesis studied by incorporation of ³H-proline into non-dialyseable material. Collagen was estimated by analysis of conversion of ³H-proline to ³H-hydroxyproline. No effect of two different PMFs, varying only in negative width, was observed on cell proliferation. Protein synthesis was not affected during exponential growth, but was significantly elevated (~6-60%) by one particular waveform. Collagen was also relatively increased; approximately 11% of the total protein being represented by collagen in treated cultures, compared with 5% in controls. Collagen types were unaffected by PMF. Both control and treated synthesized types I and III in a ratio of 9:1, with trace amounts of type V. Concurrent with this increase in protein synthesis, was an 80% increase in the amount of labelled material precipitable with antiserum to fibronectin, in treated cultures. These data suggest that certain PMFs can alter protein metabolism and in particular the accumulation of connective tissue components by tendon fibroblasts in culture, but only during the confluent phase of growth. In addition, not all waveforms have the same biological effect.

0572 A GENERALIZED THEORETICAL APPROACH TO THE DETERMINATION OF LOCAL FIELD PARAMETERS DURING CAPACITIVELY COUPLED ELECTRIC STIMULATION IN VIVO (MEETING ABSTRACT). (Eng.) Vresilovic, E. J. (Dept. Bioengineering, Univ. Pennsylvania, Philadelphia, PA 19104); Pollack, S. R.; Brighton, C. T. In: Transactions of the Second Annual Meeting of the Biological Repair and Growth Society, held on 20-22 September 1982, in Oxford, England; 2:10; 1982 (2 refs).

Dielectric, circuit, and control theory were used to develop a generalized theoretical approach to the determination of local field parameters during capacitively coupled electric stimulation *in vivo*. A generalized capacitively coupled *in vivo* experiment places the limb of an animal between two stimulation electrodes to which a driving signal is applied. These electrodes may be on the skin or separated from it by air or another material. Generally, an *in vivo* experiment is found to have a less accurately defined environment when compared to its *in vitro* counterpart. This holds true for modeling geometries and electrical properties as well. The model must approximate the actual geometry and also adequately define the boundary conditions needed to solve the Laplace equation. However, animal limbs represent complex geometries and approximate models must be used. Additionally, these models are further complicated by animal to animal variation. The electrical properties, the conductivity and the permittivity, must be defined as a function of frequency for each material. Electrode-dermal impedance may be conveniently thought of as the electrode impedance coupled to the skin impedance. The electrode-dermal impedance for humans is primarily dependent on electrode type, area, current density, signal frequency, stimulation location, and sweat gland activity. Electrode-dermal impedance has not been fully described for other species, and the applicability of the human impedance model raises questions based on the species variation in skin morphology. The relationship of the LFPs to the driving signal is established by solution of the Laplace equation with Laplace Transform methods once the system is modeled. This results in a transfer function in the s frequency-domain which is used to define the LFPs as a function of the driving signal in the time domain. The *in vivo* theoretical approach is illustrated with an experiment where 1.5-cm diameter stimulation electrodes were placed on the medial and lateral surfaces over a fibular fracture in a rabbit. A 10-V 60-kHz signal was applied with 50% amplitude modulation. Using human electrode-dermal impedance values, the calculated maximum values of field and current density were 15 V/cm and 1.5 mA/cm², respectively.

0573 FREQUENCY WINDOWS IN STIMULATING A CELL WITH ELECTRIC FIELD: A COMPUTER SIMULATION (MEETING ABSTRACT). (Eng.) Ridella, S. (Consiglio Nazionale delle Ricerche, Istituto Circuiti Elettronici, Via Opera Pia, 11 - 16145, Genova, Italy); Drago, G. P.; Marchesi, M. In: Transactions of the Second

Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:11; 1982.

The effects of an electric field on the cell membrane were investigated using a computer simulation. A cell, simulated by a multilayer spherical structure on a digital computer, was exposed to an alternating current electric field. The electrical properties of possible biological interest, such as, fields, voltages, currents and ion densities were evaluated throughout the cell to elucidate which part of the cell is stimulated and what kind of charge transport will occur. Every layer was characterized by data on complex dielectric constant or equivalent impedance, which was obtained through experimental measurements. The cell membrane model was developed to obtain the ion densities at the surface and the ion-flux across the membrane. The nucleus was modelled so as to account for the binding of divalent ions to the DNA fixed charged phosphate groups. With an applied field of 200 V/m it was found that: (1) the ion density variation on cell membrane reached a maximum (about 2%) in the frequency range 0.1-10 Hz, with possible consequences on membrane receptors and, consequently, on biological behavior; (2) the voltage on the membrane reached a maximum of 1 mV in the frequency range 1 kHz-1 MHz; a safety threshold of 1 mV had been suggested; (3) the ion passive flux and the vicinal ion concentration reached a maximum of $7.8 \times 10^{-2} \text{ A/m}^2$ and $6.9 \times 10^{-6} \text{ coulombs/m}^2$, respectively, in the frequency range 0.1 kHz-1 MHz, the frequency range used in bone-healing; (4) the absorbed ion density reached a sharp maximum of $10^{-9} \text{ coulombs/m}^2$ in the frequency range 0.1-1 Hz; the frequency range in which strong calcium ion efflux/influx has been observed; (5) current density in the nuclear membrane pores reached a very high and sharp maximum of 44 A/m^2 in the frequency range 1-10 MHz; it has been estimated that currents of this order can modify chromatin; (6) the charge shift inside the nucleus, which could influence chromatin decondensation, had a maximum at about 7 kHz. It is concluded that some electric fields inside the cell are greater than external ones at particular frequencies and that each transfer function between one of the electrical quantities of biological interest to the external field shows a maximum in the range 0-10 MHz.

0574 INDUCED ELECTRIC POTENTIALS IN VIVO PRODUCED BY CAPACITIVELY COUPLED SIGNALS (MEETING ABSTRACT). (Eng.) Brager, M. D. (Dept Orthopaedic Surgery, Sch. Medicine, Univ. Pennsylvania, PA 19104); Brighton, C. T.; Pollack, S. R. In: Transactions of the Second Annual Meeting of the Biological Repair and Growth Society, held on 20-22 September 1982, in Oxford, England; 2:12; 1982 (1 ref).

Induced electric potentials *in vivo* produced by capacitively coupled signals were investigated. The subjects for this study were six, 3-4 kg adult male

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New Zealand white rabbits and four adult male humans. The humans were patients who had electrodes inserted for treatment of ununited fractures and consented to participate in these measurements made prior to connection of the direct current power supply. The electrodes were 1.2-mm diameter stainless steel wire insulated except for a 1.3-cm tip that was implanted in bone. Two of the same electrodes were percutaneously inserted through the lateral and medial femoral condyles of the rabbit right hind limb. These were then advanced into the femoral canal in a parallel fashion along the lateral and medial endosteal surfaces. The implanted tips acted as probes for monitoring induced potentials (V_i). Bare, stainless steel capacitor plates were applied to the skin on opposite sides of the limb external to the location of the uninsulated monitoring tips. The plate diameters were 3.0 cm for human studies and 1.7 cm for rabbit studies. A function generator supplied sine wave driving signals (applied voltage, V_A) to the capacitor plates. Induced potentials in RMS voltage were measured directly across the exposed portions of the electrodes (monitoring electrodes) using a digital voltmeter. Increase in V_A always resulted in a linear increase in V_i . Limb size had no significant effect on V_i . Increasing plate diameter resulted in no significant difference in V_i . Increasing plate pressure against the skin in rabbits resulted in an increase in V_i . Through a sequence of V_A 2, 5, 10, 20 and 30 V peak-peak, loosely applied plates (determined by minimum stable current draw in capacitor plate leads) produced a mean V_i of 15.5 mV. Through the same sequence of V_A , tightly applied plates (determined by maximum stable current draw in the capacitor plate leads) produced a mean V_i of 52.5 mV. The total range of V_i was 0.5 to 168.0 mV. A monotonic increase in V_i was observed with increasing frequencies of 0.1, 1.0, 10, 20 and 60 kHz. V_A , plate size, and plate pressure were kept constant during these measurements. Measurements of remote V_i were made with the capacitor plates in locations of the body away from the monitoring electrodes. In humans the largest falloff of V_i occurred within 20 cm from the coupling site. In rabbits, at V_A of 5.6 V peak-peak the mean local V_i was 3.9 ± 1.3 mV while the mean remote V_i (plates on the opposite hind limb) was $.55 \pm .19$ mV. Therefore, the ratio of the mean local V_i to mean remote V_i was 7.1 to 1. It is concluded that the relationship between the induced or stimulating signal and the signal applied to the capacitor plates is influenced by a variety of experimental variables which must be controlled for definitive experimentation.

0575 HELMHOLTZ COIL - CELL SYSTEM SPATIAL RELATIONSHIP AND ELECTRICAL DOSAGE IN THE ELECTROMAGNETIC MODULATION OF TISSUE GROWTH AND REPAIR (MEETING ABSTRACT). (Eng.) McLeod, B. R. (Dept. Electrical Engineering and Computer Science, Montana State Univ., Bozeman, MT 59717); Pilia, A. A.; Sampsel, M. J. In: Transactions of the Second Annual Meeting of the Biological Repair and Growth Society, held on 20-22 September 1982, in Oxford, England; 2:13; 1982.

The spatial distribution of pulsating electromagnetically-induced current (PEMIC) in physiologic saline was quantitated for the most commonly employed cell culture and suspension system as a function of coil orientation. Theoretical predictions were based on Maxwell's field equations for cylindrical (coils horizontal) and rectangular (coils vertical) geometries. Computer data were generated from the theory so field plots could be done to graphically illustrate how current density changes with position. Experimental verification utilized specially constructed electrode probes with which both the induced electric fields, E , and current density, J , vectors were measured in saline. The results showed that, for cylindrical geometry, E and J were concentric rings about the center of a Petri dish or culture tube placed anywhere in the region of spatially constant magnetic field, B . Both E and J increased linearly with radius, r , having maximum values at the outermost ring, just inside the insulating vessel wall. For vertical coils, E and J vary in the vertical direction approximately linearly with saline height, h , for planes not adjacent to the vessel walls. The complete induced field pattern for this geometry was complex. However, on the bottom of a dish where most cells reside in a culture experiment the majority of J lines were perpendicular to B . Electrical dosage in a cell culture experiment, therefore, clearly depends upon coil orientation, the dimensions of the vessel, and the height of the culture medium. For example, compared to J at any r for cylindrical geometry, its value on the bottom plane for vertical coils differed by approximately the factor $h/2r$. All of the above considerations are summarized using theoretical and experimental current density-position plots. The essential results indicate that nearly uniform electrical dosage is achieved only when the cell system is relatively planar (cell culture - vertical coils). All other cases result in a spatially variable induced current density, with maximum dosages depending on coil orientation.

0576 A NEW PROCEDURE FOR ELECTRICALLY STIMULATING CELLS IN CULTURE (MEETING ABSTRACT). (Eng.) Liboff, A. R. (Naval Medical Res. Inst., Bethesda, MD 20814); Halverson, B. A. In: Transactions of the Second Annual Meeting of the Biological Repair and Growth Society, held on 20-22 September 1982, in Oxford, England; 2:14; 1982.

A novel capacitive, noninvasive procedure for electrically stimulating cells in culture is reported. The procedure has the capability of (1) allowing simultaneous study of many cluster plates, (2) mimicking the waveshapes induced by pulsed electromagnetic field coils, (3) allowing simple control of frequencies, and (4) accurately characterizing the charge density applied to the cell substrate. The excellent electric permittivity associated with tissue culture cluster plates allows one to use the wall capacitance to intrinsically differentiate pulses applied to the outside of the plates; monolayer cell

cultures plating the interior of each well are thereby subjected to precisely the same charge signature. In these studies, 24-well COSTAR tissue cluster plates were used which have a well bottom thickness of 1 mm and a dielectric constant of 3.3. These plates were modified by painting silver electrodes on the outside bottoms of all wells, experimental and control. Pulses from a function generator and a pulse-shaping circuit were applied to the plates directly in the incubator. Preliminary results have been obtained for two distinct experiments; one testing the effect of repetitive (15 Hz) electric pulsing on cell adhesion and the other measuring the effect on cellular metabolism. Human foreskin fibroblasts (HEM-HFS-15) were used throughout. Enhanced rates of adhesion and increased uptake of radiolabeled thymidine, uracil and proline were observed for negative pulses generating surface charge densities of 4 pC/cm²/pulse.

0577 ON THE TREATMENT OF LOOSENING OF ENDOPROSTHESES BY MEANS OF PULSING ELECTROMAGNETIC FIELDS (MEETING ABSTRACT). (Eng.) Kraus, W. (Inst. Medical Physics, Augustenstrasse 41, D-8000 Munich 2, W. Germany); Lechner, F.; Ascherl, R.; Blumel, G. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:15; 1982.

A clinical multicenter study including 13 orthopaedic surgery clinics and 10 private orthopaedists was performed to evaluate the use of electrical and electromagnetic stimulation in the treatment of patients with loosened endoprostheses. Low frequency (12-22 Hz, 30 Oe), sinus pulsing magnetic fields were used to treat 462 patients with cemented prostheses and 15 with cement-free prostheses. All patients were candidates for reoperation. Adjustable and special shaped coils around the hip joints were applied and the treatment was performed on an average of 2-3 hr/day for 15.4 wk with a maximum observation period of 8 yr. Treatment results were staged according to spontaneous pain, pain in motion, use of crutches, distance of walking, and dose of analgesics. In 122 (26%) of the patients excellent results were recorded, i.e., painless walking without the use of crutches was obtained, and in 188 (41%) good results were yielded; 97 (21%) reported no effects. In 55 (12%) of the cases in which treatment failed totally, patients underwent further surgery with a re-implantation. Thus, in 67% further surgery could be avoided, even in intractable cases. Comparison with previous studies indicated that the efficacy of the treatment seemed to be significantly better in cases of loosened cement-free prostheses. This treatment should be limited to cases in an early stage of loosening. Septic loosening, fractured cement, broad radiolucent lines and dislocation of the implant must be treated surgically.

0578 PULSATILE ELECTROMAGNETICALLY INDUCED CURRENTS SYNERGIZE WITH POLYMER IMMUNOMODULATING DRUGS IN THE INHIBITION OF GROWTH OF MURINE MALIGNANT MELANOMA (MEETING ABSTRACT). (Eng.) Pilla, A. A. (Bioelectrochemical Lab. Dept. Applied Chemistry and Chemical Engineering, Columbia Univ., New York, NY 10032); Norton, L.; Tansman, L. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:16; 1982.

Inhibition of the growth of murine malignant melanoma with the combined application of pulsatile electromagnetically-induced currents (PEMIC) and polymer immunomodulating drugs was investigated. One hundred female BDF₁ or BCF₁ mice were implanted with 1 mm³ B16 melanoma. The animals were then divided into control, PEMIC alone and PEMIC + Pyran (75 mg/kg, 1 or 7 days after implantation) groups. Mice treated with PEMIC were placed (free roaming) in specially constructed cages between horizontal Helmholtz air-gap coils activated for 12 hr/day. This coil configuration allowed electrical dosage to be relatively independent of animal movement. The pulsating magnetic field (dB/dt approx. = 0.1 G/usec) induced 1 Hz currents configured of 50 msec bursts of 250 usec main polarity and 4 usec opposite polarity asymmetric rectangular pulses. The average induced current per pulse could be varied from approximately 0.1-1 uA/cm³ (i.e., average pulse current per unit volume of treated tissue) while maintaining all other pulse parameters constant. Results were obtained by assessing palpable tumor volumes as a function of time and by observation of survival time. The median survival time for control animals was 7 wk and was not affected by PEMIC or Pyran alone. However, treatment with PEMIC + Pyran increased survival time to 10 wk in 100% of treated mice. This represents a significant reduction in tumor growth rate, possibly via enhancement of immune response. These results provide strong evidence that an effective and non-toxic anti-cancer treatment modality may be at hand.

0579 THE SIDE EFFECTS TO THE INTERNAL ORGANS OF PULSING ELECTRO-MAGNETIC FIELDS (MEETING ABSTRACT). (Eng.) Ohashi, T. (Dept. Orthopaedic Surgery, Murakami Memorial Hosp., Gifu Coll. Dentistry, 1-6 Wakamiya-cho, Gifu, Japan 500); Inoue, S.; Sasaki, H.; Ashihara, T. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:17; 1982.

Complications involving internal organs were investigated following exposure to pulsing electromagnetic fields (PEMF). One group of rats was exposed to PEMF while housed in a plastic cage while a second group, which served as control, was maintained in an identical cage without exposure. Following sacrifice, the abdominal organs of the rats were examined histologically and the results were compared according to the

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age of the animal, i.e., young, young adult and adult. Vacuolar degeneration was observed in the kidney and liver of rats stimulated continuously for 2 days with PEMF; the effect was age-dependent with the severest degeneration found among the younger rats. The same degree of vacuolar degeneration was observed in the liver, but not the kidney, of animals exposed 12 and 16 hr/day, resp., for 1 wk. Liver degeneration in rats exposed for 3 days was not reversed after 11 days of non-stimulation. The spleen, testis, and skin were not affected by PEMF. The results indicate that great care should be observed when applying PEMF to the spine or pelvis.

0580 TREATMENT OF AVASCULAR NECROSIS OF THE FEMORAL HEAD WITH DIRECT CURRENT: A PRELIMINARY REPORT (MEETING ABSTRACT). (Eng.) Steinberg, M. E. (Dept. Orthopaedic Surgery, Univ. Pennsylvania, Sch. Medicine, Philadelphia, PA); Brighton, C. T.; Tooze, S. E.; Hayken, G. D.; Steinberg, D. R. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:18; 1982.

The effectiveness of direct current stimulation as a supplement to surgical decompression and bone grafting in the treatment of avascular necrosis of the femoral head was investigated. Initially, 250 cases of avascular necrosis, including 48 hips treated non-operatively, 7 treated with drilling/decompression, and 9 treated with decompression and grafting, were reviewed. Seventeen hips were treated by decompression and grafting with either of two techniques of electrical supplementation. In one, 4 wire cathodes were inserted around the central graft and connected to an external power source. In the other, a single cathode was coiled about the graft and connected to a subcutaneous power pack; 10 uA were delivered to each electrode. Hips were evaluated preoperatively at 3, 6, 12 and 18 mo. Of 48 hips treated non-operatively, 42 showed progression. All 7 hips treated with drilling/decompression and 7 of 9 treated with grafting progressed, although these groups did better than the non-operative group. To date, none of the hips treated with electrical stimulation have progressed and 5 have shown healing of cystic areas. Most have noted pain relief and one has achieved a significant increase in motion. Electrical stimulation as a supplement to decompression and grafting, gives a significant improvement in the results obtained by surgery alone. Although this is a preliminary report and longer follow-up will be needed for definitive conclusions, the present results are promising and may have important clinical implications.

0581 SELECTIVE IN-VIVO CELLULAR STIMULATION WITH A DIRECT CURRENT - A PRELIMINARY REPORT (MEETING ABSTRACT). (Eng.) Schmidt, R. G. (McKay Orthopaedic Surgery Res. Lab., Dept. Orthopaedic Sur-

gery, Univ. Pennsylvania, Philadelphia, PA); Freidenberg, Z. B.; Brighton, C. T. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:19; 1982.

Results obtained using a novel design for electrical stimulation *in vivo* to determine if a selectively applied direct current could induce bone formation in muscle or cause any other cellular effects are reported. Selective *in vivo* stimulation was applied by securing a 26-gauge multistranded cathode wire inside a diffusion chamber (Millipore Corp., volume 130 μ l, pore size .45 microns) implanted ip in adult New Zealand rabbits. Each rabbit contained 1 sc implanted battery packs, each of which supplied 3 separate cathodes with a constant direct current of 5 uA. Autogenous muscle was instilled into each of the chambers at the same cellular concentration of 3.10⁶ cells per chamber in the form of a cellular suspension. Three rabbits for a total of 36 chambers were studied. Rabbits were sacrificed at 7, 13, and 18 day intervals. Two chambers from each animal (1 stimulated, 1 control) were processed histologically while the remaining 10 chambers were analyzed biochemically. Of the six chambers analyzed histologically (3 control, 3 stimulated) no difference could be detected in cell morphology or in the amount of muscle regeneration. None of the chambers demonstrated any osteoblastic activity on hematoxylin-eosin, saffronin-O, or alkaline phosphatase stains. Of the 30 chambers analyzed biochemically, no difference could be detected in protein or DNA content between stimulated and control chambers. Control and stimulated chambers demonstrated the same degree of cell growth with time. This new technique for electrical stimulation allows for the *in vivo* determination of the effects of a direct current on any isciatible cell type.

0582 SIMILARITY OF PIEZOELECTRIC PROPERTIES OF DRY BONE AND POLED POLYMERS (MEETING ABSTRACT). (Eng.) Williams, W. S. (Dept. Ceramic Engineering, Univ. Illinois, 105 S. Goodwin Ave., Urbana, IL 61801) In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:20; 1982 (6 refs).

The objective of this study was to understand why the signals produced by cantilever bending of dry bone are so large, independent of orientation of the specimen, linearly dependent on the bending moment about the electrodes, and not predictable from a piezoelectric d-matrix which adequately describes the response to uniaxial compression; an explanation was also sought as to why poled sheets often have a larger than expected converse effect (bending deflection with applied electric field) and also display the direct response features described above for dry bone. It has recently been shown that the piezoelec-

tric response of dry bone to cantilever bending can be understood on the basis of a spatially-varying value of the appropriate d-coefficient, within the framework of the classical third tensor theory of piezoelectricity: $P_i = d_{ijk}(x,y,z)t_{jk}$. This spatial variation is justified by the finding of a radial component of the spontaneous polarization. The rectangular geometry of a beam cut from a radially poled cylinder (whole bone) requires a spatial variation of the polarization between the electrodes placed on either side of the beam in the cantilever bending apparatus. Integration of the electric field, now a function of position, between the electrodes yields a predicted voltage that has the characteristics observed. A spatially-varying value of the converse-effect coefficient has been shown to explain the large deflections observed with polymer "benders." It was found that with electrically-inhomogeneous specimens, bimorph behavior can be duplicated with "monomorphs." (The bimorph analogy was invoked earlier to explain bone behavior, and the validity of the equations produced was confirmed with these ceramic devices.) Thus the puzzling piezoelectric response of synthetic polymers (PVF₂) and natural polymers (collagen) to inhomogeneous stress can be explained on the basis of specimen inhomogeneity.

0583 IN VITRO MEASUREMENTS OF BIOLOGICAL IMPEDANCES (MEETING ABSTRACT). (Eng.) Tuerlinckx, B. (Electricite Generale CP. 165; Univ. Libre Bruxelles, Ave. F-D. Roosevelt, 50, B-1050 Brussels, Belgium); Henrotte, J-L.; Rybowski, L.; Dierickx, M.; Hinsenkamp, M.; Burny, F. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:21; 1982.

The induced currents and fields in the area adjacent to a bone subjected to electromagnetic stimulation were calculated. In order to obtain realistic results, accurate and reliable impedance values for bone and muscle (both transverse and longitudinal) and fatty tissues over the same frequency range as the stimulation signal had to be obtained. A sophisticated measurement technique was therefore developed, which features: fast measurement (less than a msec) for "quasi *in vivo*" conditions; low amplitude, wide spectrum input current signal (4-20 uA, 100 Hz to 2 MHz); well-defined current flow geometry; a 4-electrode system, cancelling the effects of electrode impedance; a high-performance output voltage differential amplifier; discrete-time domain transfer function analysis; and, microcomputer controlled measurement and data acquisition. The collected data are processed by a CDC-Cyber computer, using a maximum likelihood method, and results are validated by several statistical hypotheses tests, giving a high degree of confidence in the final values. The equipment was first tested with reference R-C networks, showing excellent overall reliability and accuracy ranging from .5 to 5%. Measurements on salt water

and physiological saline proved the absence of parasitic electrode effects, and confirmed the expected accuracy. Impedance values for several biological materials were then obtained, including blood, muscle and bone, and compared with previously published values. The results include: optimum order of transfer function; transfer function parameters (Laplace and Z-transform); equivalent network parameters; standard deviations and confidence intervals for one measurement; standard deviations between different samples; and evolution of parameters in time.

0584 ON THE ORIGIN OF STRESS GENERATED POTENTIALS IN WET BONE (MEETING ABSTRACT). (Eng.) Salzstein, R. (Dept. Bioengineering, Univ. Pennsylvania, Philadelphia, PA 19104); Pollack, S. R. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:22; 1982 (2 refs).

The origin of stress-generated potentials (SGP) in wet bone was investigated with particular reference to the fluid influence on the form, magnitude and time dependence of the measured SGP. SGP measurements were made as a function of time on 6 cortical bovine femoral samples in step-loaded four-point bending. From classical streaming potential theory, the zeta potential of bone was proportional to $-(SGP)(\text{fluid viscosity})(\text{conductivity})/(\text{dielectric permittivity})(\text{outer fiber strain})$ for four-point bending of bone. For the 6 samples, the value $\zeta=0$ occurred in a range between $M=.152$ and $.337 \text{ g-mol/L}$, the crossover range. Bone is porous, possessing Haversian and Volkmann's canals, canaliculi, and a porous matrix. Therefore, the zeta potential of bone may not be a single-valued parameter, but may be a function of the local composition of the bone and the fluid at their interface. Accordingly, the zeta potential will vary spatially and with fluid ion concentration. At low concentrations ($\zeta < 0$), component A is observed at high concentrations ($\zeta > 0$), component B is observed. For concentrations near the crossover range, both components A and B may be expected. A spiked component, perhaps piezoelectric in nature, is expected at the exact crossover concentration ($\zeta = 0$). The observed SGP will be composed of these 3 components each of a given magnitude, depending upon the bone architecture and the fluid dynamics within the bone.

0585 FACTORS INFLUENCING HEALING IN THE TREATMENT OF NON-UNION WITH ELECTRICITY (MEETING ABSTRACT). (Eng.) Brighton, C. T. (Dept. Orthopaedic Surgery, Univ. Pennsylvania, Sch. of Medicine, Philadelphia, PA 19104); Friedenberg, Z. B.; Black, J.; Heppenstall, R. B.; Esterhai, J. L. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:23; 1982.

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The cases of 382 patients with non-union secondary to trauma treated with constant direct current were reviewed to determine those factors that influenced the healing rate. The patient population consisted of 231 males and 151 females of average age 38.7 yr and with an average duration of the non-union of 2.5 yr. There were 392 non-unions in the 382 patients. Forty-three percent of the original fractures were open, 66% of the non-unions had been operated on previously, and 22% had a history of osteomyelitis at the non-union site. Forty-seven percent of the non-unions were hypertrophic and 13% atrophic, 40% were neither or were mixed; the "classical" mortar and pestle configuration was uncommon (3%); 12% of the non-unions contained a synovial pseudarthrosis (the humerus showed the highest incidence of this, 41%); a non-union "scar" remained in the medullary canal in 13% of the healed patients; and the majority of tibial and femoral non-unions were sclerotic or of normal density, and the majority of humeral non-unions were osteoporotic. Factors that adversely affected healing were: (1) presence of synovial pseudarthrosis (healing rate 0%); (2) interfragmentary gap greater than one-half the diameter of the bone (healing rate 2%); combined thickness of the cortices (either proximal or distal to the non-union site) of less than 20% of the total width of the bone at that level (healing 25%); osteoporosis of the ends of both fragments at the non-union site (healing rate 29%); and (5) osteomyelitis at the fracture site (healing rate 61%). The age of the patient, the duration of the non-union, and the presence of pre-existing metallic fixation devices did not affect the heal rate. The overall heal rate for those patients treated adequately with direct current was 81%. Heal rates for the individual bones were as follows: metatarsal, malleolus, fibula, and talus - 100%; radius - 93%; tibia - 86%; carponavicular and ulna - 82%; femur and clavicle - 71%; and humerus 54%. Complications were few and consisted mainly of mild irritation around the cathodes at the skin level in those patients who were too active with the casted extremity. No deep infections occurred in this series. It is concluded that the treatment of non-union with direct current is as effective as bone graft surgery with a much lower risk/benefit ratio.

0586 TREATMENT OF NON-UNION WITH CONSTANT DIRECT CURRENT (MEETING ABSTRACT). (Eng.) Ahl, T. (Dept. Orthopaedic Surgery, Danderyds Hosp., S-182 88 Danderyd, Sweden); Andersson, G.; Herberts, P.; Kalen, R. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 1:24; 1982.

A series of 20 non-union cases are presented which were treated with constant direct current at Sahlgrenska Hospital and Östra Hospital in Gothenburg and at Danderyds Hospital in Stockholm, Sweden. Three to four teflon-coated Kirschner wires, which acted as cathodes, were inserted percutaneously into a non-

union area. A small portable battery delivered a constant direct current of 20 uA/cathode. During 12 wk of electrical treatment the non-unions of the lower extremity were immobilized in a non-weight bearing plaster cast. Casts were also used for the upper extremity except in 3 cases with non-unions of the humerus where a Hoffman external apparatus was used. Only fractures that were not clinically healed within a minimum of 9 mo and that had not shown any further signs of healing on x-ray during the last 3-mo period were included. The bones involved included the tibia in 12 patients, the scaphoideum in two, the femur in one and the humerus in four patients. One unsuccessful fusion of the ankle was also included. The duration of non-unions ranged from 6.5 to 43 mo, with a mean duration of 17 mo. Two of the non-unions were originally open fractures. Four non-unions had been operated on earlier in unsuccessful attempts to achieve union, and three patients had a previous history of deep infection. Of 20 patients treated, 9 achieved solid bone union. However, most of the non-unions of the long bones did not heal until 6-12 mo after the beginning of electrical stimulation. The tibia was the easiest bone to treat, while the humerus seemed to be the most difficult, an experience which agreed with other reports. Minor complications such as broken and dislocated Kirschner-wires and superficial skin irritation were observed in 9 cases. One patient with a previous deep infection experienced a recurrence of osteomyelitis and one patient with a non-union of the scaphoideum without previous infection developed a deep infection after 9 wk of treatment. Electrical stimulation of non-unions is considered to be a promising complement to accepted surgical therapy, especially in cases not suitable for surgery. This study also indicates that all types of non-unions do not respond well to electrical treatment.

0587 ROENTGENOGRAPHIC OBSERVATION OF ELECTRICAL CALLUS FORMATION IN CLINICAL CASES (MEETING ABSTRACT). (Eng.) Inoue, S. (Dept. Orthopaedic Surgery, Murakami Memorial Hosp., Gifu Coll. Dentistry, 1-6 Wakamiya-cho, Gifu, Japan 500); Ohashi, T.; Kajikawa, K.; Tada, M.; Saito, Y. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:25; 1982.

Approximately 40 cases of non-union or delayed union were treated with electrical stimulation using stainless steel cathodes and stainless steel or carbon fiber anodes. Roentgenographic analysis of the electrical callus formation in these cases indicated that the shape and size of the callus were not uniform. Some cases showed callus formation all around inserting and projecting areas of the cathode. Other cases showed callus formation in either part of inserting and projecting areas of the cathode. Some showed no significant callus formation at the cathode site, but gradual filling appeared at the fracture site and callus formation was found at the pin site of the ex-

ternal skeletal fixation apparatus. It is not known why the different types of electrical callus are formed. The electric potential distribution and current between cathode and anode are too complicated *in vivo* to clarify even with a computed simulator. Results of experiments using rats indicate that the callus is formed by proliferation and differentiation of periosteum and endosteum promoted with electric stimulation. It is postulated that electrical callus is formed at the most proper area of electric current and potential distribution.

0588 ELECTROMAGNETIC FIELDS USED IN THE TREATMENT OF FRESH FRACTURES OF THE RADIUS (MEETING ABSTRACT). (Eng.) Wahstrom, O. (Dept. Orthopaedic Surgery, Univ. Hosp., Linkoping, Sweden) In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:26; 1982.

The effect of extremely low frequency (ELF) electromagnetic fields (EMF) on the healing activity of fresh fractures was investigated. Thirty women (50-70 yr old) with extra-articular, dislocated fractures of the distal radius underwent routine treatment with closed reduction and immobilization in a cast for 4 wk, and were then randomized into a therapy and a control group. The therapy group was treated during immobilization with EMF in the ELF range (<1000 Hz) by means of a copper wire coil and a battery-powered current-generator. Scintimetalical examinations were performed 1, 2, 4 and 8 wk after the initial trauma, with ^{99m}Tc-diphosphonate used as a tracer. The results obtained after 2 wk showed a significantly ($p<0.01$) higher increase in scintimetric activity over the fracture area in the EMF-treated group compared to the control group ($p<0.01$). The serial scintimetric examinations indicated that EMF-treatment gave a significantly higher increase at the beginning of the healing process ($p<0.01$) and there was probably also a retrogression toward normal values faster in the therapy group than in the control group. The results indicate that treatment of fresh fractures with EMF of this type is efficacious.

0589 THE USE OF THE DENHAM EXTERNAL FIXATOR IN CONJUNCTION WITH ELECTROMAGNETIC INDUCTION OF FRACTURE HEALING (MEETING ABSTRACT). (Eng.) Simonis, R. B. (Rowley Bristow Orthopaedic Hosp., Pyrford, Woking, Surrey, England); Good, C.; Cowell, T. K. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:27; 1982.

Results are presented using pulsed electromagnetic fields (PEMFs) combined with Denham external fixation (compressed to provide rigidity) in the treatment of

bone fractures. Eleven patients had non-union of the tibia, 2 of the forearm and 1 had a failed fusion of the knee. The average time of non-union was 27 mo (10 to 55 mo). The Stimulator consisted of a waveform generator, high current output stage and treatment coil. The coil was in two flat circular sections of diameter 18 cm, mounted so that the spacing could be adjusted from a few cm to approximately 25 cm maximum. The waveform generator provided a pulse train of prf 4 kHz, duty cycle approximately 90% modulated by a second pulse train of prf 25 Hz, duty cycle 7.5%. This provided a composite waveform consisting of 3 msec duration bursts of the 4 kHz pulses at intervals of 40 msec. During each cycle of the 4 kHz pulse train, the output stage produced a magnetic field in the coil rising linearly to a peak value of around 3 mT in 230 usec, followed by decay to zero in approximately 20 usec. All the cases, except one, united within an average of 4 mo (3 to 3 mo). The one failure was due to human error in over compressing the fixator and refracturing the non-union. The use of an external fixator allows adjacent joints to be kept mobile and the skin to be treated, while the patient undergoes PEMFs. Subsequent to this report the technique has been used successfully for nonunions in most long bones including the femur and the humerus. This method has become the basis of a double blind controlled trial to determine the effectiveness of PEMFs.

0590 THE COMPATIBILITY OF METALLIC FIXATION WITH PULSED ELECTROMAGNETIC FIELDS (MEETING ABSTRACT). (Eng.) Bassett, C. A. L. (630 W. 168th St., New York, NY 10032); Schink, M. M.; Mitchell, S. N. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:19; 1982.

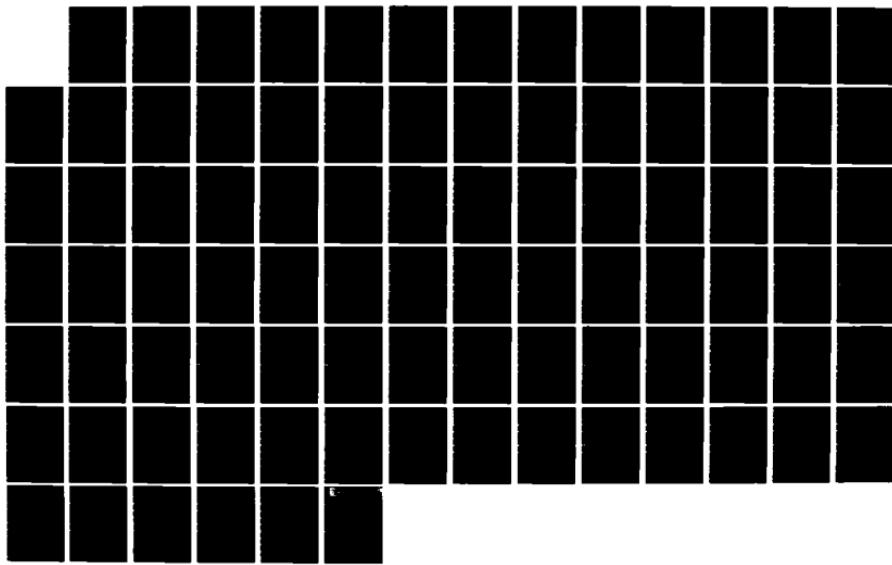
The compatibility of metallic fixation with pulsed electromagnetic fields was investigated in 540 cases of non-union. Each patient treated with pulsed electromagnetic fields (PEMFs) had a history of at least one failure to achieve union after the use of plates, screws, intramedullary rods, or pins. No patient had a concomitant surgical attempt at repair. The series included loosened, broken and distracting metallic devices. PEMFs, alone, or in combination with plaster casts and non-weight-bearing were used by the nearly 200 surgeons who contributed patients. The overall success rate was 75% and ranged from 36% for the tibia to 60% for the humerus. Twenty-nine percent had a history of infection and union occurred in 70% of these. Patients with a long disability time (2 yr) and atrophic lesions had the lowest success rate (except for the tibia). Union was determined, in part, by patient management. When hardware was loose or broken and a sound plaster cast was used, (and non-weight-bearing for lower extremities), the success rate for ill lesions (except humerus) was 93%. In the humerus, good management principles improved the percentage of union from 60%, generally, to 75%. Furthermore, patients in whom magnetogen-

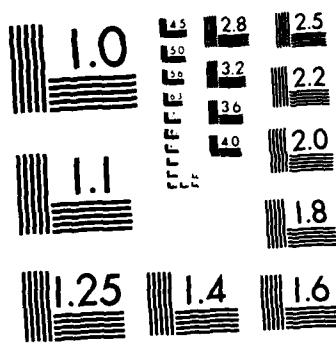
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graphic evidence of loosening appeared, around screws or rods (e.g., radiolucent zones), manifested an increasing radiodensity in these regions of bone resorption. No clinical evidence of corrosion was found and devices removed after union appeared "clean." The median time to union for all anatomical sites was 6 mo, essentially equal to that in a series of 1078 non-unions in which only 100 patients had metal in place during PEMF treatment. This study confirms the proposal that PEMFs and non-magnetic devices are compatible.

0591 THE EFFECT OF PULSED MAGNETIC FIELDS ON cAMP METABOLISM IN CHICK EMBRYO TIBIAE (MEETING ABSTRACT). (Eng.) Jones, D. B. (Strangeways Res. Lab., Cambridge, England) In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:29; 1982 (1 ref).

The effect of pulsed magnetic fields (PMF) on cAMP metabolism was studied as a mechanism of transducing electrical stimulation into cellular metabolic effects. cAMP was extracted from the separated shafts and cartilages of whole rudiments which were cultured in serum free medium for up to 8 days. PMF were applied, after the first 24 hr, in a cycle of 6 hr ON, 6 hr OFF. Although PMF had no effect on the DNA content of shafts or cartilages, PMF treated cAMP values showed large fluctuations when measured half way through the OFF period. When PMF switched OFF after 186 hr of culture, cAMP levels in shafts rose by up to 200% within 5 min, dropping to 150% over control by 30 min, and then fluctuated widely around control values for the rest of the OFF cycle. Cartilage responded to PMF OFF by dropping sharply in cAMP content to 60% of control by 5 min and then returning to a wide fluctuation around control values over the rest of the OFF period. When PMF switched ON at 192 hr, shaft cAMP values rose 150% by 5 min and then fell rapidly after 15 min to 30% of control content at 30 min, after which cAMP content fluctuated widely around control values. Cartilage showed a reverse response, dropping below control at 5 min and then increasing to a fluctuation averaging above control after 30 min. Inhibitors of phosphodiesterase (PD) were used to calculate the relative activities of PD and adenylate cyclase (Ac). These studies showed that although in shafts at 30 min into the ON period cAMP content was at 30% of control, Ac activity had risen from 0.1 pmole min per ug DNA to 0.6 pmoles min ug DNA, but this activity was exceeded by the rate of PD activity, resulting in a net loss of cAMP. Other changes in cAMP content could be explained in terms of the relative activities of Ac and PD. Trifluoperazine, an inhibitor of calmodulin was used to study the action of PMF on calmodulin in the activation of Ac and PD, and indicated that the activation of Ac and PD was calmodulin dependant. These results indicate that PMF affects cAMP metabolism through the activation of adenylate cyclase and phosphodiesterase, and effect that is

entirely consistent with the hypothesis that calcium levels in the cells are being affected. The resulting change in cAMP metabolism and the inferred change in calcium levels are also consistent with the previously reported effects of PMF on chick embryo tibiae.

0592 ELECTROMAGNETIC MODULATION OF CALCIUM UPTAKE IN EMBRYONIC CHICK TIBIA IN VITRO: DEPENDENCE ON INDUCED CURRENT WAVEFORM PARAMETERS (MEETING ABSTRACT). (Eng.) Pilla, A. A. (Bioelectrochemistry Lab., Dept. Applied Chemistry and Chemical Engineering, Columbia Univ., New York, NY 10032); Colacicco, G. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:30; 1982.

The relationship between induced current pulse parameters and short time Ca uptake in osteochondrogenic tissue was investigated. Paired tibiae were dissected from 9 day white Leghorn chicken embryos and placed in 1 cm³ of a simplified culture medium consisting of (mM) NaCl, 90; KCl, 6; CaCl₂, 1.1; MgSO₄, 1.1; glucose, 120; NaHCO₃, 10; NaHPO₄, 5; pH adjusted to 7.5, containing 0.5 uCi of ⁴⁵Ca. One of the tibiae of each pair was placed (at 38 C) between Helmholtz coils and exposed for 60 min to several induced current waveforms. Ca uptake was assessed by scintillation counting of the medium after exposure. All induced current waveforms were bipolar and approximately rectangular having pulse widths of 2-400 usec. The signals were periodic consisting of repetitive single or pulse burst patterns. The peak induced current per pulse varied between 0.1 and 10 uA/cm² as measured in the medium using specially constructed electrode probes. Ca uptake in the treated tibiae ranged to a peak of 40±7% above controls and was clearly dependent upon signal parameters. A dose effect existed versus pulse amplitude and/or repetition rate. For example, the peak response was observed for a 5 msec burst of 200 usec main, 20 usec opposite polarity pulses repeating at 15 Hz, falling off below and above this repetition rate at a constant induced current amplitude of 2 uA/cm². In addition, pulse width could be predictably varied within the range of this study provided amplitude and repetition rate were appropriately modified with little effect on the peak response. All of the results obtained in this study showed a remarkable degree of correlation with frequency analysis of the induced current waveform based upon the ion binding pathway.

0593 PHYSICAL FACTORS INVOLVED IN BIOLOGICAL RESPONSES TO PULSED MAGNETIC FIELDS (MEETING ABSTRACT). (Eng.) Jackson, S. F. (Strangeways Res. Lab., Worts Causeway, Cambridge CB1 4RN, England); Marsland T. P.; Firndale R. W.; Boutle, A. R. In:

Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:31; 1982.

Data accumulated from studies of tibiae grown in organ culture under the influence of various PEMF were correlated with information about (a) time responses and (b) amplitude and frequency content of the signals as defined by classical Fourier analysis. The processes used as yardsticks of the effects on osteogenesis and chondrogenesis included morphology, DNA metabolism/cell proliferation, changes in amounts of collagen and proteoglycan constituents and mineralization. Studies of the effect of treatment time have shown two types of response: linear increase/decrease with time, indicating a cumulative effect; or a discontinuous effect in that prolonged treatment reduced increases obtained with shorter exposure times. When different pulse train waveforms were applied under the same experimental conditions, different levels of response of one process were obtained. This finding may be related to the different energy and/or frequency content of the waveforms used. A major difference lay in the range 15-65 kHz (3 dB band width), while both 15 Hz and 4.4 kHz harmonics were common to all signals used. Comparison of the effects of repetition rates in the range of 6-133 Hz with SP waveforms, in which the signal level was maintained at a constant value, showed that a 15 Hz rate achieved the best balance between the various processes measured. Since the frequency content of the signals was similar, the observed changes may be related to differences in the harmonic spacing of the signal and/or changes in amplitude, resulting in reductions of energy. Consideration has also been given to possible field effects, so as to provide information about the relative importance of polarization phenomena versus the effects of small diffusion currents. Results also suggest that the organization/nature of the tissue may play an important role.

0594 EFFECT OF PULSED ELECTROMAGNETIC FIELDS ON CELLULAR INFILTRATION AND COLLAGEN FORMATION IN IMPLANTED VISCOSITY SPONGES (MEETING ABSTRACT). (Eng.) Jolley, W. B. (1329 Pacific St., Redlands, CA 92373); Knierim, K.; Ham, J. M.; Hinshaw, D. B. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:32; 1982.

The effect of pulsed electromagnetic fields (PEMF) on cellular infiltration and collagen formation was investigated in viscose sponges implanted sc in the rat living in PEMF for a period of 7 days. The PEMF was generated in bursts of pulses, each burst lasting 5 msec with a repetitive rate of 15/sec. The pulse rate within each burst was 3 KHz. Individual pulses had a duration of 200 usec in their principal deflection followed by a smaller deflection of opposite polarity lasting 18 usec. These pulses were applied

to two Helmholtz coils. The coils were spaced 0.3 cm apart and each had 50 turns with a circumference of 10 cm. The induced current density was about 1.1 A/cm² and established an electrical gradient of approximately 3.0 mV/cm. Four viscose sponges of nearly equivalent wt and size were implanted sc in 20 rats. The rats were randomly divided in two groups A (controls) and B (field, experimental). The rats were placed in plastic tube restrainers for periods of 20 hrs/day. Group B rats were placed between the coils of the pulsed field. Group A was kept under identical conditions except for the field. Seven days later, the rats were weighed and sacrificed. The sponges were removed and weighed. Histological reactions of the sponges were compared for the number of macrophages, neutrophils and fibroblasts present by counting 10 high power oil immersion fields in each section. Both groups of animals showed identical weight loss of 56 g during the experiment. There were no statistically significant changes in the weight of the sponges (control = 25.4 ± 0.6; field on 24.9 ± 5.1). A statistically significant ($p < 0.05$) increase in the number of fibroblasts in the PEMF (71.7 vs 54.8) was observed. The number of neutrophils and macrophages showed no statistical difference. Spectrophotometric scanning showed a qualitative difference in the collagen present using trichrome stained sections. The results of these experiments confirm data obtained by others that PEMF affect certain cells which are involved in wound healing and/or collagen formation. Further studies are in progress to define the exact mechanisms involved.

0595 MEASUREMENT OF SKIN POTENTIAL PATTERNS (MEETING ABSTRACT). (Eng.) MacDonald, N. (Dept. Electrical Engineering, Univ. Wales, Swansea, SA2 8PP, England); Watson, J. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:33; 1982 (3 refs).

Very low drift direct current silver/silver chloride electrodes were used to produce a quasi-three-dimensional display, with the axes of voltage, position, and time. An indifferent electrode was referenced to a position over the mid-diaphysis of the tibia, and eleven other electrodes were positioned proximal and distal to it. All the electrodes were interfaced to a microprocessor-controlled electrometer-type measuring instrument, and every 15 min, the set of readings was sampled. The microprocessor then plotted each point using an X-Y plotter, and interpolated continuous lines from each point in the previous set to produce the quasi-three-dimensional format. The choice of the skin surface over the mid-diaphysis as the reference or indifferent point, was made on the empirical grounds that potentials both proximal and distal to this point were normally positive. The potential pattern itself appeared to consist of "electrobiological noise" some 5 to 10 mV high, with slowly-changing peaks up to 35 mV superimposed. It

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has been noted that this pattern can be markedly altered (even to polarity reversal) by both physical and mental disturbances on the part of the subject. Plots from healthy volunteers and others are presented.

0596 THE EFFECTS OF PULSED ELECTROMAGNETIC FIELDS ON PROTEIN SYNTHESIS AND MEMBRANE TRANSPORT IN RAT SKIN (MEETING ABSTRACT).

(Eng.) Delport, P. H. (Faculty Medicine, Univ. Louvain, Louvain, Belgium); Cheng, N.; Hoogmartens, M. J.; Mulier, J. C.; Sansen, W.; De Loecker, W. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:34; 1982 (1 ref).

The effects of pulsed electromagnetic fields (PEMF) on protein synthesis and membrane transport in the skin of rats was investigated. Skin from the back of locally inbred male Wistar R rats, during the rest phase of the hair-growth cycle at 21 days of age was used after plucking of the hair. During incubation at 37°C for 5 min to 120 min a PEMF was applied to one skin sample of each rat while the other half was identically incubated outside the reach of the electromagnetic field. Driving voltage varied from 5 V to 20 V, pulse frequency from 50 Hz to 10 kHz, pulse width from 10 usec to 150 usec, pulse burst frequency from 1 Hz to 70 Hz and the number of pulses from 20 to 100. The *in vitro* stimulation of the skin by PEMF resulted in an increased incorporation of [$2-^{14}\text{C}$] glycine and of L-[^3H -alanine into the proteins only with a specific combination of parameters. The incorporation of [$2-^{14}\text{C}$] glycine or L-[^3H -alanine into the protein was increased by 40% to 90% with the PEMF characteristics: 10 V, 5 kHz (pulse frequency), 10 usec; 20 Hz (pulse burst frequency) and 20 pulses per burst. Increasing either the pulse width to 20 usec or the pulse burst frequency to 20 Hz, equally stimulated protein synthesis. The amino acid transport was enhanced by 30 to 60%. A related time curve (5:120 min) was established. Only specific combinations of pulse parameters resulted in stimulatory effects on metabolism. Thymidine incorporation to evaluate DNA metabolism did not show any clear evidence of stimulation by PEMF nor did ATP generation increase. These observations suggest that the metabolic effects of electromagnetic stimulation are probably based on mechanisms different from those observed with the direct electric currents.

0597 THE EFFECTS OF DIRECT ELECTRIC CURRENTS ON INTRACELLULAR pH AND TRANSMEMBRANE POTENTIALS IN RAT SKIN (MEETING ABSTRACT). (Eng.) Cheng, N. (Faculty of Medicine, Univ. Louvain, Belgium); Prenen, J.; Carmeliet, E.; Hoogmartens, M. J.; Mulier, J. C.; Sansen, W. M.; De Loecker, W. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:35; 1982.

The effects of direct electric currents on intracellular pH and transmembrane potentials in rat skin were investigated. After the removal of the hair by plucking, the skin from the back of 21-day-old male Wistar R rats was isolated and longitudinally halved. One half served as control and the other half was stimulated by constant direct electric currents varying from 10 μA to 10,000 μA . The tissue flaps were clamped between two adjustable stainless steel electrodes and placed in Krebs-Ringer bicarbonate buffer to be incubated for 2 hr at 37°C with and without direct electric currents supplied by a stabilized power supply. By cutting the skin in strips parallel to the electrodes, protein synthesis, ATP generation, intracellular pH and transmembrane potentials were measured as a function of the distances from the cathode and the anode and as a function of the current intensities. With direct electric currents of 100-750 μA , protein synthesis was stimulated by up to 75% ($p<0.001$) and ATP generation increased 4-5x about the non-treated controls. The highest levels of stimulation were obtained adjacent to the cathode. Near the anode the stimulatory effects on protein and on ATP synthesis were decreased by 9% ($p<0.01$) and by 68%, respectively. After electro-stimulation with 500 μA for 2 hr, a pH gradient was measured from 7.68 ± 0.04 near the cathode to 7.05 ± 0.001 near the anode. When currents passed through the tissue, the resting membrane potential was depolarized at the cathodic area, while a hyperpolarization occurred at the anode. The change on transmembrane potential was a function of the distance from the electrodes and the intensities of the current. During treatment of skin with a direct electric current, a higher anabolic activity nearer the cathodic interface appeared to be conditioned by a proton gradient and a membrane potential gradient. Proton transfer leading to ATP generation seemed to occur by a repetition of elementary proton jumps resulting in a charge transport.

0598 CHANGES IN MEMBRANE PERMEABILITY AND INTERACTIONS BETWEEN CONNECTIVE TISSUE MACROMOLECULES INDUCED BY AN APPLIED ELECTRIC CURRENT (MEETING ABSTRACT). (Eng.) Eisenberg, S. R. (Continuum Electromechanics Lab., Dept. Electrical Engineering and Computer Science, Massachusetts Inst. Technology, Cambridge, MA 02139); Grodzinsky, A. J.; Fechner, P. Y. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:36; 1982 (4 refs).

Changes in membrane permeability and interactions between connective tissue macromolecules induced by an applied electric current were investigated. Corium collagen membranes, approx. 150 micron thick, were placed in a transport cell with gradients in NaCl or pH. Collagen is nearly isoelectric at neutral pH and has (+) charge at low pH. Application of approx. 40 mV (applied current density [J] = 6.6 mA/cm²) across the membrane produced a change in intermolecular

swelling forces and concomitant isometric tensile force measured by the load cell. The possibility that matrix swelling is linked to changes in solute permeability was tested via measurement of radionuclide tracer flux ($^3\text{H}_2\text{O}$ and ^{14}C -sucrose double tracer) before and after membrane pH or ionic strength was changed directly or by means of J . The force kinetics and polarity observed suggested that an electro-diffusion process controls intramembrane NaCl concentration. Hence, changes in intermolecular spacing which affect permeability occurred in approx. 10 sec for a membrane thickness of approx. 150 um. The fact that $^3\text{H}_2\text{O}$ permeability was not significantly altered by J suggests that electroosmotic entrainment of solutes could not be the only cause for observed changes in sucrose flux. Rather, small changes in matrix intermolecular spacing can have a significant effect on the diffusivity of a larger solute (sucrose) whose size is not small compared to membrane pore radius.

0599 NERVE REGENERATION IN VITRO: CORRELATION OF CURRENT/POTENTIAL LEVELS WITH NEURITE OUT-GROWTH, NEURONAL CELL NUMBER AND AREA (MEETING ABSTRACT). (Eng.) Sisken, B. F. (Wenner Gren Res. Lab. and Dept. Anatomy, Univ. Kentucky, Lexington, KY); Barr, E. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:38; 1982.

Evidence is presented that correlates the morphological parameters of neurite outgrowth (NO) and maintenance of the neuronal population (neuronal cell areas and numbers of cells) with different direct current levels. Trigeminal ganglia, obtained from 8-day-old chick embryos, were placed in 60 mm tissue culture dishes (Falcon 3002) containing 6 ml culture media. The tops of these dishes were modified to hold either platinum electrodes, tantalum electrodes, or agar salt bridges. Potentials of -200, -400, -600, and -800 mV were imposed on dishes by employing an agar salt bridge to a saturated calomel reference electrode connected to a potentiostat. Current/voltage curves were first obtained for each metal electrode and current values alone for the agar salt electrode in the tissue culture medium. In vitro experiments on the ganglia (control cultures, cultures treated with various levels of direct current, or cultures treated with NGF, 10^{-8} M) were conducted for 3 days. Neurite outgrowth was determined semi-quantitatively in all cultures. Neuronal preservation was assessed quantitatively by counting the number of neurons in 2 micron sections of the explants on three levels and determining neuronal cell area on these sections. Neurite outgrowth was correlated with current levels rather than potential difference, i.e., maximum NO with tantalum was at -400 mV (10 nA) while platinum was at -200 mV (12 nA). Numbers of cells in ganglia treated with current (1-20 nA, any electrode) and mean neuronal cell areas were all comparable. Increased levels of current decreased both parameters. NGF treatment produced

higher numbers with larger cell areas. A comparison of each treatment to 3-day incultured trigeminal ganglia is presented graphically. It is concluded that current levels of 1-10 nA using any electrode system (platinum, tantalum, or agar salt electrodes) stimulate nerve regeneration *in vitro*.

0600 ELECTROMAGNETIC INDUCTION OF NEUROTRANSMITTER RELEASE FROM A NEURONAL CELL LINE IN TISSUE CULTURE (MEETING ABSTRACT). (Eng.) Rein, G. (St. Bartholomew's Hosp., Dept. Medical Electronics, West Smithfield, London, England); Dixey, R.; Watson, B. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:39; 1982.

The effect of low frequency electromagnetic (LFEM) fields on calcium-dependent neurotransmitter release was investigated using a neuronal cell line. Pheochromocytoma (PC12) cells grown in monolayer culture were placed in a CO_2 incubator between two concentric coils connected in parallel to a driving circuit and pulse generator producing a train of square wave pulses. A pulse width of 0.6 msec with a 1.4 msec gap between each pulse was used for all experiments, giving an overall frequency of 500 Hz. The magnitude of the resulting magnetic field applied to the cells varied from 1.6 to 8.5 G with the electric field strength in the medium ranging from +0.038 to -0.019 V/m. Noradrenaline (NA) release was measured in logarithmic phase PC12 cells by preloading synaptic storage vesicles with $^3\text{H-NA}$ taken up from the medium. After an extensive washout period to reduce cytoplasmic stores of NA, the spontaneous efflux curve was determined by measuring radioactive NA in the medium for 12 sequential 15-min periods. For the experimental runs, two culture dishes were removed from their protective Numetal shield and placed between the coils in the incubator during the 7th and 8th time periods. Release values were expressed as a percentage of total vesicular stores and normalized for direct comparison between dishes. Release values observed during LFEM field stimulation were 28% higher than control values obtained at the corresponding time points ($p<0.001$). This elevation was attributed to increased release of NA from the cells since additional experiments have ruled out the possibility that LFEM fields cause cell detachment. The addition of 15 mM Mg^{++} to the medium during the experimental periods completely inhibited the LFEM field induced release. Since magnesium is known to be a specific calcium antagonist and inhibits depolarization induced release in PC12 cells, LFEM field induced re-release is likely to be dependent on extracellular calcium. However, it remains unknown whether the release observed occurred via the same exocytotic mechanism as conventional depolarization induced release. Nonetheless, the magnitude of the effect was of the same order of magnitude as release previously shown to be induced in these cells by certain types of cholinergic stimuli. The results indicate that PC12 cells can be used as a model system for studying the

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effects of electromagnetic field on neuronal function and more specifically for studying their effects on neurotransmitter release mechanisms.

0601 THE EFFECTS OF EMBRYONIC NERVE TISSUE AND DIRECT CURRENT ON AMPUTATED RAT LIMBS (MEETING ABSTRACT). (Eng.) Sisken, B. F. (Wenner Gren Res. Lab. and Dept. Anatomy, Univ. Kentucky, Lexington, KY); Fowler, I. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:40; 1982.

The use of neural tissue implants combined with the application of direct current using bimetallic electrodes to induce partial limb regeneration in a non-regenerating vertebrate species was investigated. The right fore-limbs of male rats (inbred Harlan Fisher F344, 21-28 days old) were amputated at the mid-humeral level. Experimental animals received implants of fetal (14 day) brain or spinal cord obtained from pregnant Harlan Fisher F344 mothers. Twenty-six animals received nervous tissue implants alone; 10 animals received implants strung on tantalum wire, and 11 animals received implants strung on platinum/silver bimetallic electrodes that generated direct current. Control animals received no implant or implants of heart tissues obtained from the same rat fetuses. After implantation, the animals were housed separately. At intervals of 1, 2 and 3 mo, animals from each group were sacrificed and the limbs were x-rayed to determine the presence of new bone structures and prepared for histological examination. In the experimental groups, 13 of 26 rats which received the neural tissue alone demonstrated a positive response (presence of accessory bones with epiphyseal plates). Of the 10 rats that received the implant with tantalum wire alone, only 3 contained new bones adjacent to the original humerus. Of the 11 rats with bimetallic electrode plus neural tissue implant, none contained new bones, but 7 exhibited excessive growth of the humerus consisting of bone and cartilage. In all cases, increased amount of host nervous tissue was observed. In the control animal without neural tissue or electrodes, neither excessive growth of the host humerus or peripheral nerves, nor accessory bones were observed. The preliminary results indicate that the addition of bimetallic electrodes with neural tissue implants appears to stimulate excessive bone formation of the amputated humerus.

0602 EFFECT OF ELECTROMAGNETICALLY INDUCED PULSATING CURRENTS ON THE GROWTH CYCLE OF CHICK EMBRYO CHONDROCYTES IN CULTURE (MEETING ABSTRACT). (Eng.) Corvol, M. T. (Unité de Recherche sur les Maladies du Métabolisme chez l'enfant INSERM U. 30 Hop. Enfants Malades, 149 rue de Sevres, 75013 Paris, France); Monet, J. D.; Dautigny, N.; Assailly, J. In: Transactions of the Second Annual Meeting of

the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:41; 1982 (1 ref).

The effects of electromagnetically-induced pulsating currents (EIPC) on chondrocyte multiplication were studied *in vitro* using cultured cartilage cells from 15-day old chick embryos. The metaphyseal cartilage of tibial epiphysis was isolated by microdissection under sterile conditions and submitted to enzyme digestion. The subsequent chondrocyte suspension obtained was added to 25 ml culture flasks, each containing 100,000 cells in 4 ml Dulbecco's medium supplemented with 15% fetal calf serum. At each step of the growth cycle a group of 5 flasks was exposed to EIPC (mean induced current density = 3 μ A/cm²) between two air gap electrical coils for 2 or 3 days. Between day 3 and day 10, chondrocyte number or DNA content was not modified by a 2-day exposure to EIPC compared to controls. On the contrary, when studied between day 12 and day 20, there was a 15% increase in cell number and 33% increase in DNA per flask. The ratio of DNA per cell was not changed as compared to control flasks. Three-day as well as two-day exposure to EIPC gave a similar stimulating effect. However, this increase in the two parameters studied was never observed when the cells were continuously exposed to EIPC during the last 10 days of culture. It is concluded that short exposure to EIPC can increase cell number and DNA content in embryonic chondrocytes in culture only after these cells have initiated their DNA synthesis. No such effect is observed in non-dividing cells.

0603 SELECTED ELECTROMAGNETIC FIELD EFFECTS ON CELLULAR REGULATORY PROCESSES (MEETING ABSTRACT). (Eng.) Goodman, R. (Dept. Pathology, Columbia Univ., Coll. Physicians and Surgeons, New York, NY 10032); Bassett, C. A. L.; Henderson, A. S. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:42; 1982.

The relationship of the functional and temporal pattern of biological events in the cell to changes in the cell's electrical environment were investigated. Both biochemical and cytological methods were used to follow alterations in the pattern of genetic activity resulting from the use of pulsing electromagnetic fields (PEMFs) alone or in combination with other conditions including hormonal induction of puffs, elevated temperature (heat shock) and variation in the ionic environment. Alterations in transcription and translation were observed. These were monitored by sucrose gradient centrifugation, gel electrophoresis, isopycnic centrifugation, cytological "nick-translation" and transcription autoradiograms. Specifically, both single pulse (SP) and pulse train (PT) used over a series of time points, induced events associated with transcription. The effect of PT is a general increase in all RNA classes following -5-60

min of pulse. The most dramatic effect was observed using SP, where approximately a ten-fold increase in the specific activity of fractions of mRNA size was induced in a biphasic manner at 15 and +5 min of pulse. This was reflected in the electrophoretic pattern. These data were supported by cytological studies using either transcription autoradiograms or "nick-translation" of DNase I-sensitive regions of chromosomes. A synergistic effect was observed when SP or PT were used in combination with heat shock or hormonal induction. The results suggest that the two signals evoke distinctly different cellular responses. The role of Ca^{++} on RNA transcription patterns induced by PEMFs was determined since PEMFs are used clinically in treating avascular necrosis and non-unions. Salivary gland chromosomes incubated in Ca^{++} free media during SP or PT induction showed a dramatic increase in RNA transcriptional activity as compared with identical preparations containing Ca^{++} . The presence of Ca^{++} had no effect on RNA transcription in control preparations. The results suggest the effect of PEMFs can be directly related to transcriptional events. The induction was influenced by the type of pulse administered, as well as the cellular environment. The recognition of mediating factors in the use of PEMFs should allow a more specific determination of those conditions which are most beneficial for clinical use, as well as lead to an increased understanding of the effect of electrical fields in the normal function of the cell.

0604 ACTIN POLYMERIZATION INDUCED BY PULSED ELECTRIC STIMULATION OF BONE CELLS IN VITRO (MEETING ABSTRACT). (Eng.) Laub, F. (Dept. Membrane Res., Weizmann Inst. Science, Rehovot, 76100 Israel); Korenstein, R. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:43; 1982 (7 refs).

Actin polymerization induced by pulsed electric stimulation of bone cells was studied *in vitro*. Cells were stimulated after reaching confluence, with a series of rectangular voltage pulses (25 usec width, 3 Hz-repetition rate, 54 V/cm-amplitude in the medium) lasting for 5 min. Three types of actin could be detected on the basis of DNase I inhibition: monmeric G-actin, polymeric F-actin and a form not accessible to DNase I, which was assumed to be actin filaments integrated into some higher supramolecular network. This form is tentatively termed 'N'-actin (network-actin). In unstimulated cells, the following were obtained: 55% G-actin; 8% F-actin; and 37% 'N'-actin. Upon stimulation, this distribution changed to: ~0% G-actin; 12% F-actin; and 48% 'N'-actin. These cytoskeletal changes were related to the early changes in Ca^{2+} and cyclic AMP and suggest a possible role for the cytoskeleton in the process of stimulus transmission.

0605 ELECTROMAGNETIC MODULATION OF ENZYME FUNCTION: APPLICATION TO Na-K ATPase IN HUMAN ERYTHROCYTES (MEETING ABSTRACT). (Eng.) Pilla, A. A. (Bioelectrochemistry Lab., Columbia Univ., New York, NY 10032); Gary, K. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:44; 1982.

The relationship between the electrochemical pathways at a cell surface and the necessary signal parameters of pulsating electromagnetic current (PEMIC) to affect the rate of active transport in human red blood cells (HRBC) was quantitated. A previously reported electrochemical technique for the direct evaluation of cell membrane impedance has revealed the existence of an ion binding pathway having a time constant in the range of 10 usec. The dependence of this upon extracellular K^{+} concentration strongly suggested that this relaxation process involved Na-K ATPase. These results provided guidelines for PEMIC configuration via the consideration that a pulse width of 20 usec would be sufficient to excite (i.e., get enough current into) the Na or K ion binding pathways. A current density of 1-10 $\mu\text{A}/\text{cm}^2$ was chosen on the basis of real-time cell response. The repetition rate selected was based upon the actual Na/K exchange transport rate which is within 0.1-1 sec. Experimental measurements using Na efflux efflux rates from fresh HRBC into Na-free saline at 37°C showed that the pulse width and the amplitude range were sufficient to modulate Na-K ATPase activity with a peak increase in Na efflux of 35% at approximately 2 Hz. This enzyme is clearly the target since the PEMIC effect is ouabain inhibitable. The final correlation between the PEMIC effect and cell membrane impedance studies was achieved using frequency analysis. The results showed that all PEMIC signals constructed on the basis of a desired power into the ion binding pathway are effective for Na-K ATPase modulation. The generality of this approach was suggested by similar correlations for many *in vitro* and *in vivo* studies, including the clinical application to ununited fracture repair.

0606 STIMULATION OF MATRIX PRODUCTION BY PULSED MAGNETIC FIELDS (MEETING ABSTRACT). (Eng.) Farndale, R. W. (Strangeways Res. Lab., Cambridge, England) In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:45; 1982 (3 refs).

Pulsed magnetic fields (PMF) were applied to two biological systems to examine their potential effects on matrix turnover in skeletal tissue. Pig articular cartilage, which has served as a model of degradative processes in skeletal tissue, was maintained in organ culture for up to 14 days. Generally, PMF had no effect on glycosaminoglycan (GAG) release from the tissue, estimated spectrophotometrically in the used culture medium and the tissue, or on the incorporation

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of $^{35}\text{SO}_4$ into GAG. However, when depletion of GAG from the tissue was induced by catabolic factors in the sheep serum used to supplement the culture medium, the application of PEMF substantially prevented ($p<.01$) the release of GAG into the medium. This effect could not be stimulated by the addition of known catabolic factors, e.g., retinol, to the culture medium, and it appears that PEMF has enabled the tissue to overcome GAG depletion by increased synthetic activity. A second series of experiments used bone marrow stromal fibroblasts to determine osteogenic events could be induced by PEMF *in vitro*. PEMF did not induce these events but did stimulate the production of GAG in these cells also. Controls produced 392 μg in 5 wk, compared with 493 μg from PEMF-treated cells ($p<.005$).

3607 THE EFFECTS OF PULSED ELECTROMAGNETIC FIELDS UPON PERIOSTEAL AND OSTEOBLAST-LIKE CELLS GROWN IN CULTURE (MEETING ABSTRACT). (Eng.) Hanley, K. J. (Univ. Connecticut, Sch. Dental Medicine, Farmington, CT 06032); Norton, L. A.; Rodan, S. A. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-21 September 1982 in Oxford, England; 2:46; 1982.

The dependence of the pulsed electromagnetic field (PEMF) effect on the cellular make-up of differing calvarial cultures was examined. Cell cultures were obtained through three 30-min sequential digestions of 19-21 day fetal Sprague-Dawley rat calvaria. Through hormonal analysis, those cells obtained in the first digestion were found to be periosteal in nature, while those cells from the third digestion were osteoblast-like in nature. The periosteal and osteoblast-like cells were grown in culture in F-12 medium supplemented with 10% serum and 1% antibiotic antimycotic. Upon reaching confluence, the cell cultures were exposed for 24 hr to one of two PEMFs: Field C, a 5-msec train of 200-usec pulses, 13 usec apart repeating every 66 msec at 15 Hz, or Field D, a 5-msec train of 225 usec pulses, 28 usec apart repeating every 66 msec at 15 Hz. The two fields differed mainly in the duration and depth of the negative polarity of the signal generated, Field C having the deeper negative polarity and shorter duration. DNA synthesis was estimated by ^3H -thymidine (^3H -Tdr) incorporation. Neither PEMF had any effect upon the periosteal cell cultures. In osteoblastlike cell cultures under identical conditions, Field C enhanced DNA synthesis by 32-100% ($p<.01$). Field D had no effect upon "osteoblast-like" cell cultures. Further experimentation suggested that this effect may be due to differences in the endogenous growth rates. In "osteoblast-like" cells exposed to the PEMF under growth-limiting conditions (serum starved 48 hr prior to exposure to the PEMF), ^3H -Tdr incorporation was enhanced from 664 to 1285 cpm/ μg DNA ($p<.01$). In the same cell population exposed to the PEMF under growth stimulatory conditions (serum fed immediately prior to exposure to the PEMF), ^3H Tdr incorporation decreased from 1143 to 860 cpm/ μg DNA ($p<.02$). From

these experiments it was concluded: 1) the electrical perturbation of PEMF C has a direct effect upon osteoblast-like cells in culture; 2) the PEMF perturbations act as secondary growth regulators; 3) the effects appear to be cell and growth state specific; and 4) the PEMFs can exert bimodal effects upon DNA synthesis.

3608 MICROENVIRONMENTAL CHANGES ASSOCIATED WITH ELECTRICAL STIMULATION OF OSTEOGENESIS BY DIRECT CURRENT (MEETING ABSTRACT). (Eng.) Baranowski, T. J. (McKay Lab. Orthopaedic Surgery Res., Dept. Orthopaedic Surgery, Univ. Pennsylvania, Philadelphia, PA 19104); Black, J.; Brighton, C. T. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-21 September 1982 in Oxford, England; 2:47; 1982.

The possibility of correlating the degree of osteogenesis stimulated by direct current (DC) with specific faradic changes in the microenvironment near the cathode was investigated *in vivo*. New Zealand White adult male rabbits ($n=34$) underwent bilateral implantation of a 16-gauge, 1-cm, bare, PTFE-coated, 7-stranded 304 stainless steel wire cathode within each tibia, a 1.5 cm on edge, square, 304 stainless steel mesh anode near each shoulder, two Ag/AgCl reference electrodes, and a constant DC power supply. The electrodes and DC power supply were connected to a percutaneous multi-pin assembly that permitted interruption of the circuit and monitoring of the various electrical parameters. Finally, a device--the Multi-Puncturable Silastic Closure (MPSC)--was implanted transcutaneously at each tibial cathode to allow for insertion of needle microelectrodes through the skin and into the medullary canal. All electrodes remained for 4 wk to reduce the influence of surgical trauma. Then, the power supply was connected to one cathode and anode pair as the experimental in each animal. Three direct currents were selected: 1 μA ($n=10$), 50 μA ($n=13$), and 20 μA ($n=11$) to examine effects of, respectively, currents below, above, and within the optimum range of 5 to 20 μA previously found to stimulate osteogenesis with stainless-steel electrodes. The needle microelectrodes were coupled with an Ag/AgCl reference to produce a potential for pH and a polarization current for pO_2 determinations. The results are expressed as the ratio of experimental to control mean pH and pO_2 for wk 1, 2, and 3 and the final day of monitoring. Significant elevation of pH ($p<0.05$) occurred at 50 μA in all time periods and, to a lesser extent, at 20 μA in wk 3 and on the final day. Significant reduction of pO_2 ($p<0.05$) occurred at 20 μA in all periods and, to a lesser degree, at 50 μA in wk 3 and on the final day. No significant changes of pH or pO_2 were found at 1 μA . The large reduction of pO_2 was associated with osteogenesis at 20 μA while significant elevation of pH was coupled with necrosis at 50 μA . This investigation verifies *in vivo* a strong association between pO_2 and pH levels and osteogenesis stimulated by DC.

0609 AN IN-DEPTH SCANNING ELECTRON MICROSCOPY STUDY OF ELECTRONICALLY STIMULATED BONE GROWTH (MEETING ABSTRACT). (Eng.) Chen, T. (Pennsylvania Coll. Podiatric Medicine, 3rd and Race Sts., Philadelphia, PA 19107); Harrington, D. B.; Frasca, P.; Walter, T.; Walter, J.; Darigan, M. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:48; 1982.

Results of a scanning electron microscopy study of electronically-stimulated bone growth are presented. Tissues were taken from experimentally induced non-union canine fractures and from freshly osteotomized primate metatarsals. Some had received electrical stimulation (20 uA) and some had dummy electrodes placed at the fracture site. The electronically-stimulated samples showed a greater amount of osteoid than control samples. Newly developed bone contained more calcium and other inorganic matrix components in experimental samples than in control groups. Gold and zinc appeared in greater abundance in experimental samples than in controls. Bone appears to develop intramembranously from existing boney trabeculae, or *in situ* from fibroblasts within the internal fracture callus. In sections taken through the electrode, electrically stimulated bone appears to begin laydown in areas away from the electrode, and subsequent osteogenesis takes place in a pattern moving toward the electrode.

0610 IN VIVO GROWTH PLATE STIMULATION IN A CAPACITIVELY COUPLED ELECTRIC FIELD (MEETING ABSTRACT). (Eng.) Brighton, C. T. (Dept. Orthopaedic Surgery, Univ. Pennsylvania Sch. Medicine, 425 Medical Education Bldg., 36th and Hamilton Walk, Philadelphia, PA 19104); Pfeffer, G. B. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:49; 1982 (1 ref.).

In vivo growth plate stimulation in a capacitively coupled electric field was investigated. Seven-wk-old New Zealand white rabbits ($n=20$) were selected for uniform growth and were randomly distributed into two equal groups. A pair of 1.8×1.8 cm stainless steel capacitor plates was placed in parallel over the shaved right proximal tibial epiphyses of both experimental and control rabbits. All animals received 3 mg/kg iv oxytetracycline at the onset of the experiment (day 0) and again exactly 2 days later. Commencing with the second injection of oxytetracycline the experimental animals received a continuous 10 V pulse-pulse, ± 0 kHz symmetric sine wave signal for 3 days (days 1-4). The control animals received no electrical stimulation. Current RMS across each pair of plates was 0.54 ± 0.44 mA (0.082 ± 0.01) at the start of stimulation and 1.49 ± 0.1 mA (1.42 ± 0.03) 36 hr later. All animals were sacrificed on day 4. Longitudinal growth in 100 micron thick sagittal

sections of the proximal tibiae was quantified. The longitudinal distance between the first and second oxytetracycline labels (days 1-1) and the second oxytetracycline label and the bone-cartilage junction (days 1-4) was measured in both control and experimental animals. Each distance was calculated from the mean of twelve separate measurements taken at equal intervals across the growth plate. An eyepiece grid was used to ensure uniform specimen alignment. Ratios of right-to-left leg growth (for days 1-1 and 2-4, respectively) were established for each animal. During the 3-day stimulation period (days 1-4) an % increase in length ($p<.01$, $n=4$, group t-test) was demonstrated in the experimental group. A mean .7% increase in length was seen ($p<.05$, $n=3$, paired t-test) when stimulated growth (days 1-4) was compared to non-stimulated growth (days 1-1) in the same leg of each animal. Although several rabbits developed pedal edema there was correlation between the amount of edema and the acceleration of growth. In conclusion, this was the first evidence that a capacitively coupled electric field can accelerate longitudinal growth *in vivo*. The optimal voltage, frequency and current parameters of the signal remain to be determined. It remains clear, however, that the low voltage requirement for stimulation is promising for both safe and efficient clinical application.

0611 EXPERIMENTAL BONE HEALING INFLUENCED BY ELECTRICAL PROPERTIES AND LOCATION OF OSTEOSYNTHETIC DEVICES (MEETING ABSTRACT). (Eng.) Lagey, C. L. R. S. (Univ. Hosp., Catharynesingel 101, 3500 CG, Utrecht, Holland); Roelofs, J. M. M.; Visser, W. J.; Lentferink, R.; Duursma, S. A. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:50; 1982 (2 refs.).

The results of a study to determine whether osteosynthetic devices (i.e., stainless steel, or other electrical conductors or insulators) can influence callus formation are presented. White Wistar rats (79) underwent operations upon both femora. In order to avoid problems in reproducibility and reduction of a diaphyseal fracture, the bone lesion was realized by drilling four holes, one axial, by condylar approach, and three sagittal holes at 11, 14 and 17 mm from the intercondylar line. The diameter of each hole was 0.7 mm except for the main hole which had a diameter of 2 mm. The electrical perturbations caused by this special type of fracture were comparable to normal fracture potentials. A number of conductors and insulators were tested. Axial rods of stainless steel, platinum, polyvinyl chloride (PVC) and glass were implanted in 47 rats. Transversal transcortical pieces of PVC and stainless steel of different dimensions were implanted in 32 other rats. Callus formation was evaluated after the operation on fine grain X-rays of the pre-elevated femora and on undecalcified 100 μ m slices. Callus formation was enhanced by the pressure of each tested material in the medullary cavity. However, the bone gain was more pronounced when insular-

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tors were implanted. For the transcortical implants, however, the conductors caused more stimulation. An electrical explanation is proposed with reference to the known stimulating effect of depolarization of bone cortex versus fracture potentials.

0612 PREVENTION OF DENERVATION/DISUSE OSTEOPOROSIS IN THE RAT WITH A CAPACITIVELY COUPLED ELECTRICAL FIELD (MEETING ABSTRACT). (Eng.) Brighton, C. T. (Dept. Orthopaedic Surgery, Sch. Medicine, Univ. Pennsylvania, Philadelphia, PA 19104); Katz, M. J.; Pollack, S. R. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 1:51; 1982.

Inhibition of the development of denervation/disuse osteoporosis in the rat with a capacitively coupled electrical field was investigated. Forty (125 g) male Wistar rats underwent right-sided sciatic neurectomy (0.5-cm segment was excised) under Nembutal anesthesia. On the second post-operative day, stainless steel capacitor plates (1.5 cm in diameter) were placed over the medial and lateral aspects of the right mid-calf in each rat and held in place with tape. Lead wires from the capacitor plates were secured to the right hind limb and the abdomen by means of Velcro. The lead wires were brought out through the top of the cage and connected to a function generator in 32 of the rats and were not connected to a power source in eight control animals. The experimental animals were divided into four groups of eight rats each: group 1 was subjected to a 60-kHz, 2.5-V, peak-to-peak, symmetrical sine wave signal continuously for 12 days; groups 2, 3, and 4 were subjected to a similar signal at 5, 7.5, and 10 V, peak-to-peak, respectively. At the end of 12 days the animals were sacrificed and the tibiae and femora of each animal was excised. Results indicated that the control (neurectomized, non-stimulated) tibiae exhibited a 19% decrease in dry wt and a 17% decrease in ashed wt and control femora exhibited a 13% decrease in dry wt and a 15% decrease in ashed wt. Experimental tibiae (neurectomized, stimulated) exhibited a 6-19% increase in dry wt and a 2% decrease to 19% increase in ashed wt when subjected to signals of 5, 7.5, and 10 V, peak-to-peak. Experimental femora exhibited inconsistent prevention of osteoporosis. Mean total porosity of the tibia of non-neurectomized animals was 14%; for neurectomized, non-stimulated animals it was 51%; and for neurectomized, stimulated (10 V, peak-to-peak) animals it was 26%. It is concluded that a capacitively coupled electrical field can significantly inhibit the development of denervation-disuse osteoporosis in the rat.

0613 THE EFFECT OF DIRECT CURRENT MEDIATED BY POROUS ELECTRODES ON BONE GROWTH (MEETING ABSTRACT). (Eng.) Cheng, N. (do Dr. Muller, Acad-

emic Hosp., Dept. Orthopaedics, 3041, Pellenberg, Belgium); Delport, P.; Muller, J. J.; Nijs, J.; Wouters, J.; Sansen, W. M.; Van Raemdonck, W.; Ducheyne, P. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 1:52; 1982.

The effect of electrical stimulation on: (1) the rate and extent of new bone formation; (2) bone growth into porous implant; and, (3) the early stability of the interface between the implanted material and bone was investigated. Three groups of 5 sheep were treated with constant direct current of 10 μ A, 50 μ A and 250 μ A, respectively. A cathodic implant was placed in a 3.5-mm hole drilled in the cortical metaphysis of the distal femur, while an anodic implant was inserted 2 cm proximally. The non-stimulated control plug was implanted in the proximal tibial metaphysis of the same leg. An insulated power pack connected to the cathodic and anodic implants by Teflon-coated wires was placed sc. The animals were sacrificed at the end of 4, 8 and 12 wk. The osteogenic responses to 10- μ A, 50- μ A and 250- μ A cathodes were significantly enhanced above that of the inactive controls and the exostosis was more pronounced than the enostosis. In most instances, osteonecrosis was observed at the anodic area. The greatest cathodic osteogenesis and anodic osteonecrosis was at 250 μ A. The cause of osteonecrosis was due to the cytotoxic effect of metal ions which were released from the anodic electrode after reduction in an acidic environment. A gradient of new bone formation on the periosteal and medullary surface was observed. This was related to the distance from the electrodes, and the osteogenesis was always more pronounced at the cathodic area at 8 and 12 wk. Similar results were obtained when specimens were analyzed for bone mineral content. Although the maximal osteogenic response was at 250 μ A, the interfacial strength between bone implant was reduced significantly when compared to the controls. The early stability of the interface was not increased by any electrical treatment, as confirmed by mechanical testing. Porous electrodes offer a large surface area and thus provide a lower current density for a given current. It enables the use of a current higher than the conventional dose of 25 μ A, and thus stimulates more bone formation over a wider area.

0614 DIRECT CURRENT STIMULATION OF BONE INGROWTH IN TITANIUM IMPLANTS (MEETING ABSTRACT). (Eng.) Albrektsson, T. (Lab. Experimental Biology, Dept. Anatomy, Box 33031, Univ. Gothenburg, S-400 33 Gothenburg, Sweden); Buch, F.; Herbst, E. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 1:53; 1982.

The effect of direct current stimulation on bone ingrowth into two canals of a titanium implant was investigated. The bone growth chamber, a dividable

titanium implant, was inserted into the tibia of rabbits and a platinum anode and a titanium cathode were anchored in the bone on either side of the implant's outer periphery. Both electrodes (screws of 2 mm diameter, inserted length 4 mm) were inserted at a distance of 6 mm from the chamber. They were connected via sc-placed electrode cables to a stimulator under the skin on the back of the rabbit. The same procedure was performed on the contralateral side except that the electrode cables were not connected to the stimulator. Five chambers were stimulated with 5, 20 and 50 μ A, resp., while 15 chambers served as controls. Evaluation of the microradiograms, using an IBAS I+II computer indicated that there was more bone in the test implants compared to the control ones in 13 of 15 cases. The increase in bone formation on the stimulated side was significant at the $p=0.05$ level. In the 5 μ A-group, on the average average, there was a 79% increase of bone. All test implants contained more bone than did controls. In the 20 μ A-group, four of the test implants had more bone than did the controls in the same animal. The average bone contents in the 5 animals stimulated with 20 μ A was 202% of that of controls. In the 50 μ A-group, on the average, there was 13% more bone on the test side. In this group two of the anodes were found poorly anchored in the bone, two were found loose immediately outside the bone and one anode was relocated in the muscular tissue at some distance from the insertion place. The latter animal showed less bone in the test side compared to the control. The remaining 10 electrodes on the test side and all 15 electrodes on the control side were quite stable in the bone 3 wk after insertion. In conclusion, stimulation with 5 to 50 μ A gives a significant increase of bone formation in implants at 5 mm distance from the electrode surfaces. The experimental population was too small to determine which stimulation level gave the optimal bone response.

0615 BONE FORMATION AT PLATINUM, CO-CR, AND OTHER CATHODES (MEETING ABSTRACT). (Eng.) Spadaro, J. A. (Dept. Orthopaedic Surgery, State Univ. New York, Upstate Medical Center, Syracuse, NY 13210) In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:55; 1982.

The medullary bone response to six metal cathodes at two direct current (DC) levels was measured to investigate the reported metal-dependence of electrical osteogenesis. Seventy-four NZW rabbits were implanted with DC cathodes of Pt, Co-Cr(F-90), Ag, stainless steel (316L), Au or Ti. At least 6 animals received each type with current sources giving 0.02 and 0.2 μ A/mm² current density. Each animal received an inactive control cathode of the same material on the contralateral side. The cathodes were inserted into the medullary canal of the femoral diaphysis via a small hole in the distal metaphysis. After 3 wk, the animals were sacrificed, radiographed and the medullary new bone measured by point-counting in

microscopic cross-sections. Results which give the point counts for each case are presented graphically. Statistical analysis (student's *t*-test) of the paired data showed the most significant enhancement of new bone growth near all active cathodes and specifically for Co-Cr at 0.02 μ A/mm² for stainless steel and Ti at 0.2 μ A/mm² ($p<0.05$). The activity of Pt and Ag at 0.02 ($p<0.1$) was also noteworthy as was the growth near controls in several cases. The activity at stainless steel at higher current agrees with previous reports, but the behaviors of Pt and Co-Cr seem to be new observations. In general, bone formation at the lower current seemed to be inversely proportional to the electrode potential (as determined from polarization curves), whereas this correlation was less evident at the higher level. The results strongly suggest that current-dependent, metal specificities for electrically-enhanced bone formation do exist; expansion and repetition of this initial study is needed to verify and interpret this behavior in bone and other tissues.

0616 THE ROLE OF ELECTRODE MATERIAL AND CURRENT DENSITY IN ELECTRICAL STIMULATION OF OSTEOGENESIS (MEETING ABSTRACT). (Eng.) Black, J. (McKay Lab. Orthopaedic Surgery Res., Dept. Orthopaedic Res., Univ. Pennsylvania, Philadelphia, PA 19104); Nord, D. S.; Jones, S. B.; Dymecki, S. M.; Baranowski, T. J.; Brighton, C. T. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:56; 1982.

The role of electrode material and current density in electrical stimulation of osteogenesis was investigated. Twelve adult male New Zealand white rabbits received bilateral implantation of constant current power supplies previously adjusted to produce 20 \pm 1 μ A. Each animal received a 26 AWG, 1 cm, bare, 7 strand 304 stainless steel cathode in one tibial medullary canal and a 2.25 cm² 304 stainless steel mesh anode in the back as an active control. Group 1 (n=6) received the same power supply with a 0.38 mm diameter, 1 cm bare platinum cathode in the contralateral canal, coupled to a 2.5 cm² platinum sheet anode. Group 2 (n=6) received 0.81 mm diameter, 1 cm bare platinum cathodes and anodes identical to group 1. Current (I), interelectrode potential (IP), and anodic as well as cathodic potentials (CP) with reference to an implanted Ag/AgCl electrode were monitored 3x/wk until sacrifice on day 21. At sacrifice, the tibial medullary contents were decalcified, and the percentage of new bone in the canal was quantitated. Statistical analysis (student's *t*-test) indicated that bone growth on the control side was not significantly different in the two groups ($p<0.7$) and the grand mean (24.1%) was not significantly different from the historic mean for this model (18.8%, $p<0.25$). In group 1, with equivalent geometric current densities, the platinum electrodes stimulated 28% more new bone growth than the controls ($p<0.6$, paired) supporting the observations of others of the

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greater osteogenic efficiency of electrodes more noble than stainless steel. Bone growth with platinum in group 2 was significantly less than that for the controls ($p<0.02$, paired). More important, group 2 platinum electrodes elicited 41.4% less bone than those in group 1. This follows the change in the geometric current density (-53.1%) rather than in the cathodic potential (-5%), suggesting that current density dominates osteogenic efficiency of a particular electrode metal, given that the cathodic potential is below the limit for cellular necrosis.

0617 EFFECTS OF PULSED ELECTROMAGNETIC FIELDS ON CULTURED CHICK EMBRYONIC FEMORA (MEETING ABSTRACT). (Eng.) Noda, N. (Dept. Dental Technology, Tokyo Medical and Dental Univ., 5-45, 1 chome, Yushima, Bunkyo-Ku, Tokyo 113, Japan); Sato, A.; Isobe, Y.; Furuya, K.; Ishida, A. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:57; 1982.

The effects of pulsed electromagnetic fields (EMF) on cultured chick embryonic femora were investigated to elucidate the mechanisms and biological effects of electromagnetic stimulation. One-hundred and twenty-two pairs of femora were excised from 10- or 11-day-old chick embryos and cultured at 37°C in an atmosphere of 5% CO₂ and 95% air. One of each paired femora was exposed to EMF, with the other used as a control. The medium adopted was modified F-12 supplemented with 10% calf serum. On day 10 of cultivation, femora were measured, weighed, and examined histologically. At the end of the culture period, several femora were pulse-labelled with ³H-thymidine, ³H-proline, or ³⁵Sodium sulphate supplemented to the medium and radioactivities were analyzed by liquid scintillation counter. The EMF were characterized by a pulse train signal composed of 18-20, 200 nsec long, quasitriangular pulses lasting accumulatively 5 nsec and repeated at 11 Hz with magnetic flux density of 0.5 to 30 G. Exposures to EMF were performed continuously except in cases of ³H-thymidine incorporation. In those experiments, three different exposure modes were compared: (1) continuous; (2) 6 hr on off; and (3) 24 hr on/off. Incorporation of ³H-thymidine and ³Hproline was promoted significantly ($p<0.05$), whereas incorporation of ³⁵SO₄ was unaffected. Among the three modes, incorporation of ³H-thymidine was promoted more in the continuous and 6 hr on/off group than in the 24 hr on/off group. It is concluded that pulsed electromagnetic fields promote DNA and protein synthesis when applied continuously. Other results suggest that continuous or intermittent stimulations with shorter (6 hr) on/off intervals may promote DNA synthesis more than those with longer (24 hr) on/off intervals.

0618 BONE RESISTIVITY (MEETING ABSTRACT). (Eng.) Rinaldi, R. A. (Louisiana State Univ. Sch. Medicine at Shreveport, Anatomy Dept., P.O. Box 33932 Shreveport, LA 71130); Goodrich, J. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982, in Oxford, England; 2:58; 1982.

The electrical parameters of rabbit femur bone including resistivity were studied. Polarization of platinum electrodes embedded in both cortical and medullary bone was performed. A four-point method was used wherein the outer electrodes introduce current (0.1 to 1 V alternating current at selected frequencies from 0 to 5000 Hz) into the bones while the two inner electrodes monitor the current. The electrodes were embedded in bone cement (Surgical Tex) with the electrodes insulated from fluids surrounding the bone with Neoprene "O" rings. The electrodes were platinum (0.5 mm diameter). Measurements were made with a high impedance voltmeter and a low current ammeter which utilized minimal amounts of current in the measurements. Polarization of the outer electrode yielded resistance values that were erratic for different electrode configurations. Studies indicated that the ohmic resistance of both cortical and medullary femur bone performed at 1000 Hz and <7 V minimized capacitive reactance and Faradaic reactions at the polarizing electrodes. Cell constant measurements (at 1000 Hz) before and after death of rabbits circumvented the geometry difficulty and allowed a reasonable ohmic resistance value (minimum capacitive reactance) to be obtained. The ohmic resistance of both cortical and medullary bone was approximately 900 ohms/cm². Phase angles of 6 degrees at 40 Hz decreased to 0.8 degrees at 1000 Hz and remained constant to 7000 Hz before increasing. This corresponded to 95 ohms at 4 Hz, an error of <1% of the total impedance between polarizing electrodes at 1000 Hz. Resistance values obtained for both cortical and medullary bone resulted in an increase of near 10% after post mortem. Bone resistivity for both cortical and medullary bone increased following death of the rabbit. During anesthesia there was a slight decrease in resistance. However, upon sacrifice, heart and breathing cessation, the resistivity values climbed to the values of the live subject. Within 4 hr of death and with temperature of the animal maintained at 39°C, there was a notable (20%) increase in bone resistivity. The results indicate the existence of a physiological state which is important in determining bone resistivity.

0619 GROWTH OF CHICK EMBRYO MODULATED BY PULSED ELECTROMAGNETIC STIMULATIONS (MEETING ABSTRACT). (Eng.) Saha, S. (Biomechanics Lab., Dept. Orthopedic Surgery, Louisiana State Univ. Medical Center, Shreveport, LA 71130); Pal, A.; Reddy, G. N.; Albright, J. A. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:59; 1982 (3 refs).

Incubating fertilized chicken eggs were used in an evaluation of the effect of different pulsing electromagnetic fields on bone growth. This model system was chosen due to its low cost and ease of operation, compared to an animal model. The goal was to obtain a dose-response curve for pulsed electromagnetic fields based on the criterion of skeletal growth of chick embryo. Pulsing electromagnetic field (PEMF) of several desired shapes, amplitudes, and repetition frequencies could be produced with three specially designed and fabricated tunable pulse generators. A pulse generator was used to supply current to a rectangular coil (39 cm x 31 cm, 90 turns of 24 AWG coated copper wire) surrounding a test group of 60 fertilized chicken eggs in an incubator. These eggs were exposed to a particular pulse shape (measured by a sensitive probe) throughout their incubation period. The control group consisted of an equal number of fertilized eggs incubated separately in an adjacent room. Several embryos from both groups were examined from days 7 to 21 of incubation. The embryos were measured, weighed and their bones stained. Altogether, seven batches of eggs were examined, each batch exposed to a different pulse shape. One pulse shape with pulse width of 0.7 msec, a duty cycle of 40% and a repetition rate of 205/sec produced an increased rate of growth for the embryo and its skeletal system. However, for all other pulse shapes examined, the test group in general showed a decreased rate of growth. Bones from these test groups of embryos were also smaller compared to controls. Similarly, the bending strength of tibiae and femora from these electromagnetically stimulated embryos was less than that of the control group. The results indicate that embryonic growth can be modified by electromagnetic stimulation.

0620 OBSERVATIONS ON THE EFFECTS OF PEMFS ON IN VITRO MACROMOLECULAR MODELS (MEETING ABSTRACT). (Eng.) Anderson, A. M. (Bio-Medical Engineering Unit, c/o The Medical Inst., Hartshill, Stoke on Trent, Staffordshire, England); Hastings, G. W. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:60; 1982.

An *in vitro* macromolecular system developed to model collagen at a fracture site in bone is described. The aim was to study the effect of static and pulsed magnetic fields on the orientation of simple, well-characterized macromolecules during polymerization and thereby investigate this aspect of non-union treatment. This study will be extended to more complete synthetic collagens, and to regenerated collagen gels. Acrylamide or mixtures with methyl methacrylate, styrene or dimethylamino ethylmethacrylate, in aqueous or alcohol solution, were cast to give thin films of homo or copolymers on glass slides following initiation of polymerization by ultraviolet radiation. The samples were subjected to static or pulsed electromagnetic fields (PEMFs) before and during the polymerization process. Conventional light micro-

scopy revealed apparent gross differences between field and non-field samples. Polarized light microscopy and x-ray diffraction were used to provide more quantitative data concerning orientation and inter-molecular spacing. The range of morphologies in both sets was high, and therefore interpretation of changes was complex. However, there may be at least one minor change in low angle x-ray diffraction pattern, in samples exposed to PEMFs.

0621 COMPUTER ANALYSIS OF DATA IN 11,000 UNUNITED FRACTURES SUBMITTED FOR TREATMENT WITH PULSING ELECTROMAGNETIC FIELDS (MEETING ABSTRACT). (Eng.) Goldhirsch, A. R. (Electro-Biology International (UK) Ltd., 127-129 Southampton St., Reading, Berkshire, RG1 3 EA, England); Gaston, S. R.; Ryaby, J.P. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:61; 1982.

A study initiated >7 yr ago and designed to provide detailed information on the value of pulsed electromagnetic fields (PEMFs) in the treatment of non-unions is presented. The treatment protocol comprised the application of a plaster cast to control movement; the selection of appropriate coils and driving voltage; correct placement of the non-union within the resultant field; treatment periods of 10-12 hr daily; strict non-weight bearing for lower limb fractures during the initial stages of therapy, and a graded exercise program once signs of healing were evident. Information on every case treated with PEMFs was stored on computer to permit subsequent regular analysis of a variety of functions. Data are presented on 11,000 ununited fractures which have completed or are currently being treated with a course of PEMF therapy. The accumulation of data on a series this large has provided a unique opportunity to evaluate not only the overall success rate of this treatment modality (75%), but to examine in depth the influence of such factors as reactivity of the lesion, infection and the presence of hardware on healing rates, and the ultimate outcome of PEMF therapy. The success rate in the subgroup of patients who had not undergone any operative intervention prior to the initiation of PEMF therapy was compared with that in reported series of non-unions treated solely by surgical methods and established a case for the initial application of PEMFs as a reasonable alternative to such procedures.

0622 ELECTROMAGNETIC TREATMENT OF NON-UNION. A EUROPEAN MULTICENTER STUDY (MEETING ABSTRACT). (Eng.) Hinsenkamp, M. (Service d'Orthopédie-Traumatologie, Hopital Univ. Erasme, Route de Lennick 808, 1070 Brussels, Belgium); Ryaby, J.; Burny, F. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society,

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held on 20-22 September 1982 in Oxford, England; 2:11; 1982.

The European experience using pulsed electromagnetic fields (PEMFs) in the treatment of nonunion is discussed. Since 1977, more than 300 cases of nonunion have been treated with PEMFs in various European orthopedic centers. One of the most significant factors affecting treatment outcome is the type of nonunion, with a success rate of 67.8% reported for hypertrophic nonunion as compared with 58.1% for atrophic nonunion. Also, the anatomical location and sex of the patient appeared to have a determinant effect. The age of the patient or other historical data, however, had no important effect on treatment outcome. A comparison of the treatment response of the nonunion population of the U.S. with that of European countries indicates few differences.

1623 CHANCES AND PROBLEMS OF THE SUPPLEMENTARY TREATMENT OF CONGENITAL PSEUDARTHROSES OF THE TIBIA WITH ELECTRIC AND ELECTROMAGNETIC FIELDS (MEETING ABSTRACT). (Eng.) Ascherl, R. (Inst. Experimental Surgery, Technical Univ. Munich, Ismaninger Strasse 22, D-8000 Munich 80, W. Germany); von Finkenstein, A.; Lechner, F.; Blumel, G. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:63; 1982.

The benefits of electric and/or electromagnetic stimulation in cases of congenital pseudarthroses of the tibia are evaluated. Eight patients with congenital pseudarthroses were treated by means of electric stimulation. The cases were considered to be true congenital pseudarthroses; none of the patients suffered from neurofibromatosis or fibrous dysplasia. In seven of these cases the Kraus-Lechner system was applied in addition to surgery. One patient had been treated with pulsed electromagnetic fields. The leg of one of the patients operated on by internal fixation (electrified I.M.-rod) had been amputated; after an initial satisfying callus formation pseudarthrosis recurred again. One female patient was also retreated because of a recurrence of the pseudarthrosis. In two further cases a beginning osteolytic reaction was observed exactly in the region of the former pseudarthrosis, although after the initial treatment the bone was stable and consolidated. These patients are under therapy by means of the external pulsing magnetic field which seems to be able to prevent progressing osteoresorption. Usually the electric treatment takes much longer than in cases of acquired pseudarthroses. Four cases healed after only one further surgery followed by electric stimulation. In cases of congenital pseudarthroses additional treatment by electric fields seems to be helpful, but is not as successful as in cases of non-unions.

0624 TREATMENT OF CONGENITAL PSEUDARTHROSIS OF THE TIBIA USING A CONSTANT DIRECT CURRENT (MEETING ABSTRACT). (Eng.) Peterson, D. Dept. Orthopaedic Surgery, Adelaide Childrens Hosp., 72 King William Road, North Adelaide 5006, South Australia; Simonis, R. B. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:64; 1982.

A method of treating congenital pseudarthrosis of the tibia using a constant direct current (DC) is described. During surgery the pseudarthrosis and abnormal bone are excised leaving some shortening. The tibia is aligned and held with an intra-medullary nail (Steiman Pin), passing through the ankle joint into the os calcis. The cathode of a DC battery is inserted into the pseudarthrosis site which is then bone grafted. The implantable battery supplies 20 μ A for a minimum of 5 mo, after which it is removed. Of the 20 cases treated so far, 14 have united and 6 are still undergoing treatment. In several of the patients it has proved necessary to implant 2, and in one patient, 3 batteries before union could be achieved. One child refractured after the intra-medullary nail was removed at 1 yr; it is now recommended that the nail be left *in situ* for at least 3 yr. The shortening of the affected leg corrects spontaneously once union has been obtained.

0625 ELECTRIC RESISTANCE AND IMPEDANCE OF DOG TISSUES (MEETING ABSTRACT). (Eng.) Ohnishi, T. (Dept. Orthopaedic Surgery, Murakami Memorial Hosp., Gifu Coll. Dentistry, 1-9 Wakamatsu-cho, Gifu, Japan 500); Inoue, S.; Kajikawa, K.; Ibaragi, K.; Sasaki, H. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:65; 1982.

Electric resistances of tissues of bone, muscle and blood of adult dogs were determined by measuring interelectrode potentials *in vivo* using a 20- μ A constant electric current stimulator which had been used in clinical cases for non-union. The resistance of bone was 62 kOhm (1.23 V), muscle 40 kOhm (0.78 V), and blood 52 kOhm (1.04 V). The interelectrode potential using skin electrodes was much higher than that using bone electrodes. The impedances of tissues were obtained with a Kohlrausch bridge of 300 Hz. The impedance of bone was 140 Ohm/cm, muscle 10 Ohm/cm, blood 73 Ohm/cm, kidney 42 Ohm/cm and liver 38 Ohm/cm. Electric stimulator electrodes should be inserted into bone and insulated from soft tissues such as muscles to avoid short circuit, since muscle has a higher conductivity than bone. In this way, electric current can be obtained along the bone, and the current is effective for new bone formation. When the skin electrode is used, it should be large enough and also should have good contact to reduce electric resistance and interelectrode potentials.

0616 EXPERIMENTAL STUDY OF BONE REMODELLING INFLUENCES BY DC CURRENTS (MEETING ABSTRACT). (Eng.) Lagev, El. L. R. S. Dept. Experimental Surgery, Univ. Hosp., Katharinenziele 11, 3500 CG, Utrecht, Holland; Roelofs, J. M. M.; Lentferink, R.; Akkermans, L. M. A.; Janssen, L. W. M.; Wittebol, P. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:66; 1982.

The influence of direct current (DC) energy on bone remodelling was studied in 54 white Dutch rabbits using DC current of varying intensities and polarities. The currents were applied by platinum electrodes, the first in, the second either around the femoral diaphysis, or implanted at some distances. Currents of 20 or 3 uA were used, with potentials varying between 1.5 and 3.2 V. The maximum current density was calculated at 0.3 uA/mm² electrode surface. The results were evaluated on fine grain X-ray film, and on decalcified histological slices of ± 100 µm thickness by an image analyzer. The amount of bone found at the stimulated side was expressed as percentage of its heterolateral control. In the group of medullary anodes faced by circular cathodes a significant increase of the amount of total bone in the stimulated femur was found in the vicinity of the electrodes and also more proximally, especially for the low current density. Periosteal and endosteal bone formation were stimulated equally. However, in the groups of medullary cathodes faced by periosteal anodes, an insignificant inhibition was noted. The group of medullary anodes with distant cathodes showed no significant difference. Again a significant ($p<0.05$) stimulation of both endosteal and periosteal bone formation was observed in the group with a medullary cathode in combination with a distant anode, as well as in the group of circular cathodes with distant anodes. It is concluded that the orientation of the electrical field versus the polarity of the electrodes was not an exclusively determining factor in DC bone stimulation because both stimulation and inhibition were observed adjacent to the cathode depending on the location of the anode. However, stimulation never occurred with the cathode at a distance. The tested potentials and current intensities stimulated in a similar way. The densitometric evaluation was in accordance with the histological findings. The latter had the advantage of allowing a precise location of the bone remodelling.

0617 ELECTRICAL STIMULATION OF FREEZE-DRIED BONE ALLOGRAFTS (MEETING ABSTRACT). (Eng.) Bramham, G. B. (Dental Res. Branch, Stop #18, Naval Medical Res. Inst., Bethesda, MD 20814); Triplett, R. G.; G.; Liboff, A. R.; Yeandie, S. S. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:67; 1982.

Electrical stimulation was evaluated as a method of enhancing the repair of freeze-dried allogeneic banked bone to reduce the complexity of surgical reconstruction. Two-mm full-thickness defects were created bilaterally in the mandibular body of 12 adult male beagle dogs (*Canine familiaris*). The bone grafts consisted of 1 freeze-dried allogeneic U-shaped tray filled with freeze-dried allogeneic crushed cortical particles 1.1-1.5 mm in diameter. In one side an active platinum electrode was implanted which delivered 20 uA supplied by a constant current generator implanted beneath the skin on the dorsal surface of the neck. The contralateral side received a dummy platinum electrode without current. Output from the power pack was recorded Ix/W through a percutaneous lead. Bone repair was assessed by sequential submento-occlusal radiographs and quantitative radionuclide imaging with ^{99m}Tc-methylene diphosphonate interfaced with a medical computer at 1, 2, 4, 6, and 8 wk. End-point evaluation of repair included quantitative and subjective mobility determination and histology. Eight of 12 animals were free of complications and suitable for data analysis. Although the overall degree of healing, as evidenced by the uptake of radio-labeled diphosphonate, was only marginally improved for the electrically stimulated defects as compared to the controls, there was a clear trend in the data suggesting a peak in the effectiveness of the electrical stimulation post-operatively at 4 wk. This effect was also observed in changes in the effective resistance of the defect, which reached a minimum between 3 and 4 wk following surgery. It should be stressed that the use of ^{99m}Tc uptake in bone defects, coupled with computer-aided analysis to obtain relative levels of diphosphonate uptake, may represent the most precise method yet developed to assess the effects of electrical stimulation in bone.

0628 FLUORESCENT MICROSCOPIC INVESTIGATIONS INTO THE BONE HEALING UNDER STIMULATION WITH BI-POLAR PULSE CURRENTS AND INTERFERENCE CURRENT IN THE ANIMAL EXPERIMENT (MEETING ABSTRACT). (Eng.) Schubert, Th. (Orthopadische Klinik der Medizinischen Akademie "Carl Gustave Carus", DDR-8019 Dresden, Fetscherstrasse 74, E. Germany); Kleditzsch, J.; Wolf, P.; Beer, L.; Hellinger, J. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:68; 1982.

The effect of stimulation with bipolar pulse currents and interference current on bone healing was investigated. Cross-bred rabbits of either sex were osteotomized on the left proximal third of the tibia. The animals were stimulated using the bipolar square-topped pulse current procedure (1 Hz and 10 Hz, respectively ± 25 and ± 50 A, respectively, intensity, permanent stimulation) or the interference current procedure (oscillation frequency 100 Hz, intensity 1 mA, 4 hr daily). An osteotomized group served as control. The undecalcified bone sections were

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quantitatively measured in the area of the periosteal and endosteal accumulation seams as well as in the area of the Haversian canals and compared by means of multiple variance analyses. A consensual reaction was found in all animals within the region of the opposite side intracortically. A delay in the Haversian remodelling within the first 1 wk was found in the animals which were osteotomized only. This delay could not be detected in all electrically stimulated groups. In the interference current procedure, there were saving reactions within the region of the periosteal and endosteal areas of the opposite side with massively increased accumulation within the stimulating region. The electrical stimulation lead to a shortening of the fracture healing period by skipping the physiologically occurring delay of the Haversian remodelling in fractures and osteotomies.

0629 TECHNICAL PROBLEMS OF THE IMPLANTABLE BONE STIMULATORS (MEETING ABSTRACT). (Eng.) Guttler, P. (MTE, Medizinische Akademie "Carl Gustav Carus," DDR-3019 Dresden, Fetscherstrasse 74, E. Germany); Kleditzsch, J.; Hellinger, J. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:69; 1982.

Technical problems encountered in the use of implantable bone stimulators are discussed. Implantable stimulators and the electrodes attached thereto must be tissue-tolerated and corrosion proof. The geometrical construction of stimulators and electrodes is very important as well as the optimal construction of the isolation of the fixing plates and screws when they are applied. Problems in the choice of suitable batteries are discussed.

0630 THE ELECTRICAL ENVIRONMENT PRODUCED AT BONE FRACTURE SITES BY INDUCTIVE COUPLING (MEETING ABSTRACT). (Eng.) Hart, F. X. (Dept. Physics, Univ. South, Sewanee, TN 37375); Marino, A. A. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:70; 1982.

The results of a calculation to yield the dependence of the electric field and current density upon the electrical properties of the bone and adjacent soft tissue, bone and soft tissue geometry, and characteristics of the applied magnetic field are presented. Application of Faraday's Law of Induction and the requirement of continuity of the total current density (conduction plus displacement) at the bone soft-tissue interface yields an expression for the electric field of the form, $E = A sin(\omega t - B cos(\omega t))$, for applied sinusoidal field, and, $E = C(\exp(-t/\tau))$, for pulsed-field applications, where A, B, and C are complicated functions of the conductivities and permit-

tivities of the bone, soft tissue, and overall tissue geometry, and τ is the pulse rise time. The variation of the electric field, and the resulting current density have been calculated for a variety of applied magnetic fields. The data demonstrate the effect of frequency and pulse rise time on the electrical environment at the fracture site. The nature of the changes in the electrical environment (if a fixed treatment procedure) as the gap narrows with healing will also be described. It is hoped that the results will lead to a better understanding of how the electrical environment at the fracture site depends on the parameters of the applied field, and thus to improved treatment procedures for patients.

0631 LOW FREQUENCY PULSING ELECTROMAGNETIC FIELDS IN THE TREATMENT OF DELAYED UNIONS AND ACQUIRED PSEUDO-ARTHROSIS (MEETING ABSTRACT). (Eng.) Cadossi, R. (Centro Experimental Hematology, Univ. Modena, Policlinico, Via Del Pozzo, 41/100 Modena, Italy); Giancetti, F.; Fontanesi, G. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:71; 1982 (1 ref).

The use of low frequency pulsing electromagnetic fields (LFPEF) for the treatment of delayed unions, acquired pseudo-arthrosis and trophic ulcers is discussed. The unit utilized has high impedance coils supplied with 200-V electrical tension. The wave shape used has the following characteristics: 53 or 75 Hz frequency, 3 msec impulse length, square wave shape, rising edge in the order of magnitude of 1 usec. Patients were admitted to the protocol study only if the fracture lasted at least 6 mo with no healing. Home treatment was performed 11 hr/day. The mean length of treatment was 5 mo. Of 45 patients who completed the treatment, 41 healed while 4 had no benefit. LFPEF therapy can be considered very useful in traumatology, particularly in the case of delayed unions and acquired pseudo-arthrosis. No significant side effects were observed. The healing process appears to be mediated by a strong stimulation of periosteal callus formation.

0632 ELECTROMAGNETIC STIMULATION OF FREEZE-DRIED CORTICAL BONE GRAFTS IN RABBITS (MEETING ABSTRACT). (Eng.) Gehner, J. B. (340 Salem-Woodstown Rd., P.O. Box 137, Salem, NJ 08079). In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:72; 1982.

The effects of electromagnetic stimulation of freeze-dried cortical bone grafts were studied in rabbits. The cortical bone of rabbit femurs was stained *in vivo* with tetracycline, then harvested and freeze-

dried and used to make matched cortical grafts. Grafts were surgically implanted into adult New Zealand rabbits and "on-layed" over the lateral cortex of the uninjured femoral diaphysis. In the control group, the animals were placed in dummy coil cages 3 days wk for 6 hr/day for 10 wk. In the treatment group, the animals were placed in cages with active electromagnetic stimulation coils calibrated to give a standard wave form to the area of the femoral diaphysis. The animals were treated for the same time period as controls. The grafts were harvested and studied histologically by light microscopy, ultraviolet microscopy and scanning electron microscopy of non-decalcified cross sections of the recipient femurs with attached cortical grafts. Comparison of matched pairs revealed a significant increase in bone bridges from the cortex of the recipient to the endosteal surface of the cortical grafts and a significant advancement of the stages of "creeping invasion" and "osteogenic regeneration" of the cortical grafts.

Growth Society, held on 20-22 September 1982 in Oxford, England; 2:73; 1982.

Results in five congenital and 51 acquired non-unions of bone, stimulated using an invasive device, are reported. The unit delivered a constant but pulsed right-angled current of positive polarity measuring 20 to 25 μ A (750 mV) at a frequency of 20 Hz. The power pack encapsulated in epoxy resin was implanted at the time of operative fragment stabilization. The cathode was inserted at the site of the non-union gap. After 2 to 12 mo, all but two of the acquired non-unions and one of the congenital pseudarthroses healed. In the unsuccessful cases, the bone ends were often totally necrotic. Four cases required reimplantation because of broken wires or exhaustion of the battery, and two cases failed owing to purulent infection. Electrostimulation is an adjuvant treatment to fragment stabilization in hyporeactive and hypovascular or congenital pseudarthroses. Electrical stimuli may be assumed to simulate conditions which are essential for bone healing.

0633 IN VIVO SKELETAL MODIFICATIONS OF CHICKEN EMBRYOS INDUCED BY ELECTROMAGNETIC FIELDS (MEETING ABSTRACT). (Eng.) Rooze, M. (Laboratoire d'Embryologie et d'Anatomie Humaine, Hopital Universitaire Erasme, Route de Lennick 308, 1070 Brussels, Belgium); Hinsenkamp, M.; Duchateau, J. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:73; 1982.

Skeletal modifications of chicken embryos induced by electromagnetic fields were investigated *in vivo*. After 4 days incubation, chicken eggs were exposed to a permanent pulsed electromagnetic field for 100 or 150 hr. Both wing and leg ossification patterns were examined. On calibrated pictures total length and length of primary ossification points of the stylopodal and zeugopodal bones were measured. The results indicated: (1) no edema and no malformation in embryos submitted to electromagnetic fields; (2) electromagnetic-field-induced increase of the embryonic wt with more pronounced wt gain in cases of prolonged exposure; (3) increase in bone length, especially of the more distal segments mainly in the leg; (4) earlier onset of infection in activated embryos compared with controls; and, (5) larger ossification points of the activated embryos. The results also indicate that the position of the eggs between the coils is important and seems to illustrate a specific effect of the electric field.

0634 REPAIR OF NON-UNIONS BY ELECTRICALLY PULSED CURRENT STIMULATION (MEETING ABSTRACT). (Eng.) Zichner, L. (Dept. Orthopaedic Surgery, Univ. Frankfurt, Marienburgerstrasse 2, D-6000 Frankfurt a.M. 71, W. Germany); Scale, D. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:73; 1982 (2 refs).

0635 ELECTROSTIMULATION AND BONE LENGTHENING (MEETING ABSTRACT). (Eng.) Scale, D. (Dept. Orthopaedic Surgery, Univ. Frankfurt, Marienburgerstrasse 2, 6000 Frankfurt, W. Germany); Zichner, L. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:73; 1982.

Clinical and experimental findings concerning electrostimulation of bone growth are reviewed and preliminary results of one ongoing study, which assumes polarity to be the active principle underlying electrostimulation, are presented. In an investigation employing rabbits, the anode was inserted into the epiphysis and the cathode into the metaphysis and vice versa. Retardation of bone growth (7/10 rabbits) was observed in both experiments, while two animals showed accelerated bone growth and one, no difference.

0636 TREATMENT OF NON-UNION OF THE FEMUR WITH PULSED ELECTROMAGNETIC FIELDS (MEETING ABSTRACT). (Eng.) Delport, P.; (Univ. Hosp., B 3041 Pellenberg, Belgium); Mulier, M.; Cheng, N.; Mulier, J. C. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:73; 1982.

The results of a study using pulsed electromagnetic fields in the treatment of non-union of the femur are presented. Two Helmholtz coils were placed on the outer surface of a cast. Treatment was applied for 10-14 hr/day until clinical and radiological evidence of union was present. Controlled axial compression

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exercises with progressive loading started when osseous bridging of the gap was observed radiologically. Treatment was applied to 15 difficult fractures of the femur in which non-union had been present for at least 3 mo with an average duration of 3 yr. Sepsis was present in six patients and most had undergone the operations. Union was achieved both clinically and radiologically in 13 of the 15 femur fractures with a mean time of 10 mo treatment with PEMF. Two were failures (1 amputation and 1 after radiotherapy). It is concluded that PEMF therapy is simple, safe and avoids hospitalization. This method is preferred in cases of recalcitrant non-unions of the femur.

1637 PHYSICAL ASPECTS OF PULSED MAGNETIC FIELD STIMULATION (MEETING ABSTRACT). (Eng.) Marsland, T. P. (Strangeways Res. Lab., Wort's Causeway, Cambridge CB1 4RN, England). In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 1:77; 1982.

The electric and magnetic fields generated by field coils driven by pulsing currents were investigated. Study of the free space field problem divides into two areas: spatial dependence and time dependence. The spatial dependence of the magnetic and electric fields was studied theoretically using a vector potential treatment. The resulting integral equations were evaluated with a computer program, and the fields plotted for various coil geometries. Experimental measurements of the magnetic fields were made with a Hall probe. They are in close agreement with the calculated values--of the order of 1-20 mTesla (peak). Electric field values were derived from search coil measurements on Helmholtz-aiding field coils which also are in good agreement with calculated values. The time dependence of the voltages induced in a small search coil were studied, and the waveforms were further characterized by their frequency domain representation via classical Fourier analysis. This analysis has formed the basis for the design of a series of new pulsed field generators, whose biological effects are currently under investigation. The fundamental question of the interaction between the fields and the biological material was approached. Small perturbation models were used to approximate the induced current distribution within materials exposed to pulsed magnetic fields.

1638 SEM OF S. AUREUS ON CURRENT-ACTIVATED SURGICAL PINS COATED WITH SILVER AND SILVER STEARATE MONOLAYERS (MEETING ABSTRACT). (Eng.) Colmano, G. (Veterinary Medicine Res. Center, VPI & SU, Blacksburg, VA 24061); Fainter, L. K.; Edwards, S. S.; Barranco, S. D. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 1:79; 1982.

S. aureus (3×10^6 colony forming units), which had been introduced in the femurs of rabbits on the surface of stainless steel pins coated with monomolecular films of silver (Ag) stearate activated by 12 mA positive direct current cm^{-2} for 1 hr, were killed. The effects in vitro (blood agar) on control, positive, and negative current treated pins and surrounding agar were observed by a scanning electron microscope (SEM) and showed that: (1) more bacteria were present on positive than negative current-treated stainless steel electrodes; however, more bacteria appeared in the negative than in the positive current-treated agar; (2) fewest numbers of bacteria were on the negative current-treated solid Ag electrode and agar; bacteria on positive current-treated agar were in possible erythrocyte pits; and on the positive electrode surface the bacteria appeared deformed; (3) bacterial growth was heavy on control and negative current-treated solid tarnished (oxidized) Ag electrodes and agar; the growth was less heavy on the positive current-treated electrode and agar; (4) bacterial growth was uniformly low on all Ag stearate-coated (by evaporation) electrodes and agar (greatest on control); bacteria on negative current-treated electrode appeared swollen but not in negative current treated agar; (5) greatest reduction of bacterial growth was seen on the positive current-treated Ag stearate monomolecular films-coated electrode and agar; (6) growth was sparse on all Ag electroplated electrodes (no agar sample available); (7) bacterial growth was heavy on control Ag electroplated chlorided electrodes and agar; pitted areas of positive current-treated electrode were free of bacteria while growth on agar was heavy; both negative current-treated electrode and agar showed minimal growth.

1639 SPECIFIC UHF FREQUENCIES FOR CELLS STIMULATION AND HEALING PROCESS (MEETING ABSTRACT). (Eng.) Feilus, V. M. (19 rue du Docteur Arnaudet, 92190 Meudon, France). In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 1:80; 1982.

A new electric current and/or electric field generator was developed, which employs the highest frequency compatible with international specifications, body tolerance during repeated long-term exposure, and optimal effectiveness. The apparatus was designed to deliver energy at 0.5 mW/cm^2 , which is well within the respective safety standards of the U.S. and U.S.S.R. The machine employs a UHF antenna and features a double spiral antenna which can be applied directly to the skin.

1640 ELECTRICAL STIMULATION OF THE SPINAL CORD AFTER CORDOTOMY TO INCREASE SURFACE TEMPERATURE (MEETING ABSTRACT). (Eng.) Rinaldi, R. A.

(Louisiana State Univ. Medical Sch. at Shreveport, P.O. Box 3392, Shreveport, LA 71130). In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:81; 1982 (2 refs).

The increase in surface temperature following electrical stimulation of the spinal cord was investigated. Complete cordotomies were performed at L2 in four adult rats (2 male, 2 female). One wk was allowed for animals to recover from surgery and hair was removed with a commercial depilatory agent from lower limbs and ventral body surface. Ten sites were selected for surface temperature measurements. The electrical stimulation was with platinum electrodes (0.5 mm in diameter) activated by a watch battery plus a resistor which produced a current of 0.5 to 1 μ A at 0.5 to 3 V direct current. All selected temperature areas were measured with the stimulator on or off with a 30-min interval between to allow for adjustments of the subject to experimental or control conditions. A thermistor probe (YSI #4098) designed to be taped on the skin measures temperature change. This thermistor had a time constant of 1.1 sec, the time required for the thermistor to read 63% of a newly imposed temperature change. Approximately 5 "time constants" were required for the probe to determine 99% of the total temperature change. This thermistor was attached to a tele-thermometer (YSI #43TK) to obtain temperature readings. Each reading required approximately 5 min. The results are presented graphically. There was an average increase of temperature of the body surfaces measured from 0.27 to 0.91°C. This was the first study to measure direct electrical stimulation of the spinal cord and the resultant temperature changes on the body surface in animals.

0641 A PILOT STUDY OF A CASE OF LONG STANDING DEGENERATIVE O.A. (OSTEO-ARTHRITIS) OF BOTH HIPS (MEETING ABSTRACT). (Eng.) Rakshit, A. K. (128 Harley St., London W1, England). In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:82; 1982.

The use of very low frequency pulsating electromagnetic (EM) energy in the treatment of a case of osteoarthritis of both hips is presented. EM energy (field intensity, 100 G; 50 Hz) was applied initially for 20 min on alternate days, then 2x/wk, and toward the end of the course of treatment, 1x/wk. The radiological appearance of the left hip, which was the more affected, was significantly improved. In the right hip, the radiological appearance was almost normal. It is concluded that EM irradiation helps reverse the pathological changes of osteoarthritis in the early stage of its development.

0642 CLINICAL EXPERIENCE WITH ADDITIONAL POST-OPERATIVE ELECTROMAGNETIC STIMULATION OF PSEUDARTHROSES (MEETING ABSTRACT). (Eng.) Wiendl, H. J. (Unfallchirurgische Klinik Allgemeines Krankenhaus, D-8600 Bamberg, W. Germany). In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:83; 1982.

Experience in the application of postoperative stimulation with electromagnetic alternating fields in 67 cases of pseudarthroses of long tubular bones and in 4 cases of osteotomies by use of an implanted coil according to the Kraus-Lechner method is presented. The cases include: 12 pseudarthroses of the femoral neck, 12 of the femur, 30 of the tibia, 5 of the humerus and 8 of radius or ulna. In about a quarter of the cases there were infected pseudarthroses, partly with larger defects. A precondition of the treatment was a regular osteosynthesis with plates, nail or fixateur externe in the greater part combined with autologous bone graft. Postoperative stimulation with electromagnetic field was performed on the average of 6-8 wk for 4 hr daily, and in some cases longer. The 4 osteotomies healed quickly without problems. In most of the pseudarthrosis cases there was complete consolidation of bone, especially in the problem cases such as pseudarthroses of the femoral neck or defect-pseudarthroses with inflammation. Seventy-six percent of all patients had previously undergone one or more operations without success. In 90.5% of the patients application of electromagnetic stimulation after surgery resulted in complete bone bridging. In 4.7% of the cases success was obtained after changing the procedure once more with renewed stimulation. Only in 3 cases (4.7%) was the treatment ineffectual.

0643 THE EFFICACY OF ELECTRICAL STIMULATION ON EXPERIMENTALLY INDUCED NON-UNION FRACTURE OF THE CANINE TIBIA (MEETING ABSTRACT). (Eng.) Harrington, D. (Pennsylvania Coll. Podiatric Medicine, Philadelphia, PA 19107); Walter, J.; Walter, T.; Chen, T.; Bodamer, W.; Black, D. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:84; 1982.

A new method of creation of an experimental non-union fracture model is presented and the results of an investigation of the biological events in electrically-stimulated closure of a non-union fracture are reported. Forty-five mature adult pure-bred Beagle dogs were divided into three groups: Group A consisted of animals receiving bilateral tibial osteotomies wherein one leg served as a control and the other leg served as experimental. Groups B and C each received unilateral osteotomies with Group B serving as experimental animals and Group C serving as a control. An initial surgical procedure (Phase I) was designed to create a non-union fracture, while in a second proce-

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dure (Phase II), control or experimental electrodes were inserted into the non-union gap. The post-surgical duration of Phase I was 56 days, and the post-surgical period for Phase II was 38 days. Each surgical area was x-rayed immediately after creation of the non-union, at the end of Phase I, at the beginning and at the end of Phase II. Samples were retrieved at the end of Phase II and prepared for histology or scanning electron microscopy. Samples were studied microscopically to determine the quality and nature of the tissue-types appearing in the surgically created defect, degree of vascularity and the qualitative assessment of new osteoid and bone. Control sections showed only small amounts of bone formation, whereas new bone appeared extensively in the electrically stimulated samples. Samples prepared for scanning electron microscopy were observed for tissue morphology, type of new bone, level of ossification, and specific mineral concentration and localization. These studies confirmed a greater rate of osteogenic activity and ossification in experimental samples versus controls. X-ray studies throughout Phase I and II concurred with the histological and scanning electron microscopy data.

0644 THE EFFECT OF CROSS-LINKING ON STRESS-GENERATED POTENTIALS (SGPs) IN TENDON (MEETING ABSTRACT). (Eng.) Steinberg, M. Z. (Dept. Orthopaedic Surgery, Univ. Pennsylvania Sch. Medicine, Philadelphia, PA 19104); Unger, A. S.; Jimenez, S. A.; Bashey, R. L.; Pollack, S. R. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:85; 1982.

The effect of cross-linking on stress-generated potentials (SGPs) in tendon was investigated using dry specimens to eliminate the role of streaming potentials. Thirty-two sections of canine flexor tendon were divided into two experimental and two control groups and treated for 24 hr at 22°C with formaldehyde (pH 7.3) or glutaraldehyde (pH 9.5), both active cross-linking agents. Controls were treated with the appropriate buffer alone. After thorough drying, specimens were subjected to 4-point bending in an electrically shielded climate chamber with serial deformations of 75 to 175 microns. Potentials were measured from opposite surfaces with platinum electrodes and were recorded simultaneously with load and deformation. There were no differences between the electrical waveforms or the polarity generated by treated and control specimens, both of which were similar to moist whole bone. The voltages, however, were significantly elevated by treatment with both formaldehyde and glutaraldehyde. Analysis of load/deformation curves showed that treated specimens were "stiffer" than controls. Increasing the number of crosslinks in tendon collagen by treatment with formaldehyde or glutaraldehyde caused a significant increase in SGP. It may therefore be postulated that the naturally occurring crosslinks of collagen play a role in the generation of potentials by tendon

and bone. It cannot be determined from these studies whether this is a direct or indirect effect, but it is presumably independent of streaming potentials.

0645 FREQUENCY DEPENDENCE OF THE ELECTRICAL IMPEDANCE PROPERTIES OF COMPACT BONE (MEETING ABSTRACT). (Eng.) Saha, B. (Biomechanics Lab., Dept. Dept. Orthopaedic Surgery, Louisiana State Univ. Medical Center, Shreveport, LA 71130); Reddy, J. N. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:86; 1982 (3 refs).

A differential technique was employed for accurate determination of the specific resistance and capacitance properties of compact bone for a wide frequency range. A gain-phase meter (Hewlett Packard, Model 3575A) was used in a reference reading to estimate the wiring and cable capacitance. A second measurement was made with a bone specimen. From the difference of the two readings (magnitude and phase of an output to input voltage), it was possible to calculate the resistive and reactive components of bone impedance. These values were verified by taking another set of independent readings with an LCR meter (Hewlett Packard, Model 4262A). The measurements were repeated at several frequencies starting from 1 kHz to 1 MHz. For higher frequencies, the impedance values showed a decrease with increasing frequency. The specific resistance (R) was 7.56 kOhm/cm and the specific capacitance (C) was 0.166 nifarad/cm for fresh bovine longitudinal compact bone specimens. The impedance properties were direction dependent showing the anisotropic nature of bone. The calculated impedance values based on R and C values measured at one frequency agreed well with the measured values for other frequencies. The result indicates that by using the differential technique, errors due to stray capacitance can be eliminated while measuring the dynamic impedance properties of bone.

0646 ON THE MECHANISM OF BIOLOGICAL CONDUCTION (MEETING ABSTRACT). (Eng.) Cheng, N. (Dept. Biochemistry, Univ. Louvain, 300, Louvain, Belgium); Hoogmartens, M. J.; Mulier, J. C.; Sansen, W. M.; De Loecker, W. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2:87; 1982.

The mechanism of biological conduction was investigated by examining the direct current (DC) conductivity of rat skin. Fresh skin strips from the back of rats were isolated, weighed and clamped at both ends with a pair of stainless steel electrodes. Resistance and voltage measurements were made immediately with an electrometer. Following the initial measure-

ments a new set of readings of the skin strips were taken after drying and weighing. Similarly, the subsequent readings at different time intervals during drying were recorded. The resistivity of the skin was thus measured as a function of water content. The flow of current (charge transfer) was roughly estimated by the change of proton concentration (the rate of protonation and deprotonation) which was monitored by the pH change of cellular homogenate. It was found that the resistivity of the skin increased almost linearly as the wet wt of the tissue decreased. The DC conductivity observed was a function of water content of the skin. Protons were produced at the anodic area and consumed at the cathodic area during the passage of DC. The rate of proton production was equal to the rate of proton consumption as confirmed by pH measurement. The results of DC conductivity as a function of water content and the change of proton concentration after oxidation or reduction of H₂O at the interfaces suggest that water molecules are the most predominant electron donors or acceptors undergoing charge transfer reactions. It is likely that the conduction process following electrochemical reactions at the electrodes depends on the availability of water molecules. With the application of a weak direct current, water molecules are protonated (H₂O + H⁺ = H₃O⁺) after donating electrons to the anode and deprotonated (H₃O - H⁺ = OH⁻) after accepting electrons from the cathode. During a reaction at the cathodic interface electrons are added and protons removed in equal numbers. Similarly protons are added and electrons removed at the anodic interface.

1047 A GENERALIZED THEORETICAL APPROACH TO THE DETERMINATION OF LOCAL FIELD PARAMETERS DURING CAPACITIVELY COUPLED ELECTRIC STIMULATION IN VITRO (MEETING ABSTRACT). (Eng.) Vresilovic, E. J. (Dept. Bioengineering, 119 Towne Bldg./D3, Univ. Pennsylvania, Philadelphia, PA); Pollack, S. R.; Brighton, C. T. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2: 38; 1982 (2 refs).

A theoretical approach is presented, which allows the determination of the local field parameters (LFPs), electric field and current density, *in vitro* and *in vivo*, respectively. Fundamental electrical engineering principles from dielectric, circuit, and control theory were applied in the development. A generalized *in vitro* experiment includes a biological sample cultured in a vessel containing medium. Generally this vessel is placed between metal electrode plates, to which a driving signal is applied. While the driving signal is commonly given as the electrical stimulation parameter, the apparatus geometry and the electrical properties, the conductivity and the permittivity of the materials as a function of frequency have a determining effect on the actual values of the LFPs during an experiment. To calculate these LFPs, the experimental system must be modeled to allow solution of the Laplace equation with properly defined boundary

conditions. Obviously, if electrical forces are to affect cell function, it is through their interaction with charge in the cell or in the local environment of the cell. LFPs are the fundamental quantifiable parameters, and they are the parameters to which a cell should have a predictable response. After consideration of the geometry and the electrical properties, the relationship between the driving signal and the LFP is established by solution of the time dependent Laplace Equation using Laplace Transform methods enabling simpler frequency (s) domain solutions. This results in the definition of a transfer function, F(s), such that F(s) = LFP(s)/DS(s) where LFP(s) is the local field parameter of interest and DS(s) is the driving signal. The time domain solutions of the LSPs are readily obtained by inverse Laplace Transformation. This theoretical approach was applied to an experiment where chick chondrocyte cell cultures are stimulated with a 1750-V 5-Hz square-wave. The resulting field and density have maximum values of 50 uV/cm and 0.75 uA/cm², respectively. A second application to the experiment in which rat costochondral junction tissue cultures were stimulated with a 5-V 50kHz signal resulted in a 150 uV/cm field and a 2.4 uA/cm² density at 50 kHz. Although the driving voltages in these two experiments were separated by over two orders of magnitude, the calculated LFPs agreed to within a factor of 3 although their time dependences differed.

1048 THERMAL CONSIDERATIONS IN ELECTRICAL STIMULATION (MEETING ABSTRACT). (Eng.) Liboff, A. R. (Oakland Univ., Dept. Physics, Rochester, MI 48063). In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 2: 89; 1982.

Attempts are underway to determine the energy dissipation per unit volume J.E and the associated temperature increase using a commercially available stimulator (EBI/OSTEOGEN system) that generates a pulsed signal. In the initial series of experiments polystyrene flasks in different orientations containing 25 ml of culture medium (DMEM) were irradiated for periods of up to 10 min. The entire apparatus was totally enclosed in styrofoam. The temperature was monitored continuously using a fine fluoroptic probe which was completely non-metallic, thereby preventing any chance of direct magnetic induction, as may occur with thermocouples or thermistors. Results to date indicated that the temperature increase in the irradiated medium was no more than .05 °C (the present temperature resolution) but that the inductive coils themselves were being heated to at least 0.1 °C, for signal repetition rates of 25 Hz. It is expected that the temperature resolution will shortly be improved to better than .001 °C. Additional experiments are planned on rats. It should be noted, however, that *in vitro* substances offer the possibility of a more measurable change than might occur *in vivo*, given the additional tendency to temperature regulation

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resulting from the vascular system.

determining the effect of various electromagnetic radiations.

1649 THE EFFECT OF ORIENTATION OF HELMHOLTZ COILS ON NEURITE GROWTH OF NERVE GANGLIA IN VITRO (MEETING ABSTRACT). (Eng.) Sisken, B. F. (Werner-Green Res. Lab., Univ. Kentucky, Lexington, KY 40506); McLeod, B. In: *Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society*, held on 20-22 September 1982 in Oxford, England; 1:90; 1982.

The effect of orientation of Helmholtz coils on neurite growth of nerve ganglia was investigated *in vitro*. Since the current density is minimal in the center of the culture dish in the horizontal orientation (HO) but maximal for vertical orientation (VO), data was collected comparing neurite outgrowth of ganglia located near the center of each dish with the ganglia in the periphery. The "center" was arbitrarily defined as the center one-third of the dish. It must be recognized that the distribution of the current density changes dramatically from HO to VO due to different boundary conditions, but on the bottom of the culture dish, some general comparisons can be made. For the HO the current density varied in a linear fashion from zero in the center of the dish to a maximum at the outer edge, while for the VO it varied nonlinearly from maximum in the center to zero at the edge. Dorsal root ganglia (5-7/dish) from 8 day chick embryos were placed in gelatinized culture dishes which were set between Helmholtz coils in the following manner: in the VO, five dishes were set one on top of the other; in the HO, two levels of four dishes each were set between the coils. The dishes were exposed to a single pulse waveform (15 mV, 325 usec positive, 20 usec negative, 72 Hz) for either 2 days (constant exposure) or for 2 days (12 hr on/off). After 3, 4, and 7 days *in vitro* the neurite outgrowth (NO) from the cultured ganglia were scored on a basis of 0 to +5 max. The results obtained appeared to depend not only on the orientation of the coils but also on the total time of exposure. After 3 days *in vitro* (3 DIV) ganglia in the center of the dishes in the VO experiments (where the current density is highest) had a higher NO score than ganglia located elsewhere. At 5 DIV, this situation was reversed, i.e., neurite outgrowth score of ganglia in the center decreased to a lower score than the rest of the ganglia. In the HO experiments, at 3 DIV, ganglia in the center of the dishes (where the current density is the lowest) exhibited a lower score there than found elsewhere. At 5 DIV this situation changed so that centrally located ganglia outscored those located in other areas. The data suggest that ganglia located in areas receiving high levels of current density from pulsatile electromagnetically-induced currents are stimulated to produce an immediate response which then decreases with time, while areas receiving lower levels of current demonstrate a slowly increasing response time. It is concluded that both current density and time serve as important parameters in

1650 THE EFFECT OF DIRECT AND INDUCED ELECTRIC CURRENTS IN RABBIT SCIATIC NERVE REGENERATION (MEETING ABSTRACT). (Eng.) Brummitt, S. S. (Dept. Biomedical Engineering, Duke Univ., Durham, NC 27706); Wachtel, H. In: *Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society*, held on 20-22 September 1982 in Oxford, England; 1:91; 1982.

The implantable nerve cuff technique was used to study the effects of applied direct currents and induced pulsed currents on regeneration in the rabbit sciatic nerve. Each nerve cuff was constructed by sewing an array of Pt-Ir electrodes into silastic tubing. Strips longitudinally, the cuff was surgically implanted around the sciatic nerve. The cuffs were normally 50-100% larger in diameter than the nerves to allow for nerve swelling as a result of dissection trauma. Stainless steel, teflon coated cables ran from the cuffs to percutaneous connectors which emerged through the skin on the animal's back. Each sciatic nerve was crushed before being loaded into the cuff. The point of crush was usually within the array of electrodes so that periodic (every 3-10 days) stimulation and recording from the nerve could reveal electrophysiological changes associated with regeneration both proximal and distal to the crush site. Due to the low impedance of nerve tissue, the system allowed delivery of the current to the entire portion of the nerve within the insulating sleeve of the cuff, which eliminated much damage to the nerve. Battery packs were plugged into the percutaneous connectors for various lengths of time to allow direct current (15 nA, 100 nA, 1 uA) to run from an electrode (anode) beneath the connector to one of the electrodes in the array surrounding the nerve. The contralateral nerve served as a control with a dummy battery pack. Typically, the nerve was stimulated to elicit a maximal compound action potential. The electrophysiological data were correlated with a muscle function test and histology. To date no significant difference in regeneration was detected between experimental and control nerves. This system can be used to study the effects on nerve regeneration of induced currents from externally applied fields. The use of such induced currents substantially decreases contamination from electrode products that occurs using direct current.

1651 EFFECT OF GAMMA-RADIATION AND HYPERTHERMIA ON DNA REPAIR AND NAD⁺ TURN OVER IN CULTURED LYMPHOCYTES (MEETING ABSTRACT). (Eng.) Jonsson, G. G. (Dept. Oncology, Univ. Hosp., S-221 85 Lund, Sweden); Pero, R. W.; Eriksson, J. In: *Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society*, held on 20-22 September 1982 in Oxford, England; 1:92; 1982 (3 refs).

Unscheduled DNA synthesis (UDS) and cellular NAD⁺ pools were investigated after exposing human lymphocytes to hyperthermia and gamma-radiation separately and in combination. UDS was measured using ³H-thymidine, which is incorporated into the DNA during repair synthesis. Nucleotides were extracted using a perchloric acid-methanol procedure followed by KOH neutralization and analytic isotachophoresis with the aid of an ultraviolet detector. DNA repair synthesis was related to NAD⁺ pools via the chromosomal enzyme poly (ADP-ribose) polymerase which was found to have a fundamental role in recognition and repair of DNA damage. UDS declined with increasing temperature. At 42.5 °C the UDS was reduced to about 30% of the values determined at 37 °C. Following gamma-radiation damage the NAD⁺ pools dropped to very low levels, but recovered to the original level within 3 hr. Moderate hyperthermia (42.5 °C) altered the kinetics resulting in slower and less effective recovery. Heat-treatment at 44 °C prior to radiation killed the cells.

ing of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 1:94; 1982.

Clinical results obtained using a self-made electrical apparatus for constant direct current stimulation of non-union is described. A power source containing a 9-V battery delivered a constant current from 1-20 uA. As a cathode one to four Teflon-coated stainless steel Kirschner wire electrodes were inserted into the pseudarthrosis region. The stainless steel anode was fixed epicutane. The applied current was 12-17.5 uA for 12 wk. Ten patients with complicated pseudarthrosis who had undergone variable pretreatment (5 tibia; 3 femur; 1 humerus) were treated with direct current stimulation. At 1 yr post-treatment, 3/5 cases of pseudarthrosis were healed. Two large defect pseudarthroses were treated otherwise. Five cases of stimulated pseudarthroses are in progress. Based on the authors' experience, direct current stimulation appears to be an effective, inexpensive, and uncomplicated method of pseudarthrosis treatment.

1651 IMMUNE RESPONSE AND ANTIINFLAMMATORY ACTIVITY OF PULSED 27 MHz WAVES (MEETING ABSTRACT). (Eng.) Zecca, L. (Dept. Pharmacology and Orthopaedics Clinic, S. Raffaele Hosp., Univ. Milan, Milan, Italy); Costi, P.; Dal Conte, G. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 1:93; 1982.

Effects on blood, immune response and antiinflammatory activity were evaluated in rats and mice after exposure to pulsed electromagnetic radiation at 27 MHz (1 mW/cm²). In rats treated 20 min per day for 20 days an increase in white cells ($p < .005$) and gamma-globulin concentration ($p < .1$) was observed. The percentage of lymphocytes decreased while that of neutrophils increased. When mice were exposed to gamma-rays (750 rad) only, the animals pretreated with the above-mentioned waves and those posttreated showed a substantially lower death rate as compared with controls. In mice treated before and after being subjected to gamma-rays, 58% survived >30 days. In another experiment, the inflammatory response to electromagnetic radiation was investigated. A group of animals was administered phenylbutazone, the other one was exposed to 27 MHz energy. In the irradiated group animals evidenced an inhibition of the inflammation rate ($p < .01$ versus controls) compared with the phenylbutazone-treated group. These results demonstrate the immunostimulatory and antiinflammatory effect of this low-intensity radiation.

1653 DIRECT CURRENT IN THE TREATMENT OF NON-UNION (MEETING ABSTRACT). (Eng.) Regling, G. (Dept. Orthopaedics (Charite), Humboldt-Univ., Scharnhorststrasse 3, 104 Berlin, E. Germany); Sippel, H. In: Transactions of the Second Annual Meet-

0654 PULSING ELECTROMAGNETIC FIELD EFFECTS ON CULTURED FIBROCYTES (MEETING ABSTRACT). (Eng.) Loyd, R. D. (Baylor Univ. Medical Center, 3600 Gaston Ave., #303, Dallas, TX); Matthews, J. L.; Newman, J. T.; Roa, R. In: Transactions of the Second Annual Meeting of the Bioelectrical Repair and Growth Society, held on 20-22 September 1982 in Oxford, England; 1:95; 1982.

The effect of pulsing electromagnetic fields on cultured fibrocytes was investigated. For a preliminary study of the responsiveness of fibrocytes to pulsed fields, a fibrocyte cell line that produces collagen in culture was selected for evaluation of the effect of pulsed electric fields on the mitotic activity of these cells for varying time periods using two units that generate different signal configurations. Stimulator Unit 1 had a repetitive pulse burst signal. The primary (positive) pulse portion was a quasi-rectangular slope with a time duration of 100 usec and a positive peak amplitude of 1.5 mV/cm. This was followed by a secondary pulse of opposite polarity with a pulse duration of 15 usec and an induced peak voltage amplitude of 44.5 mV/cm. Unit 2 had a repetitive pulse signal with the primary (positive) pulse being a quasi-rectangular slope with a time duration of 325 usec and a positive peak amplitude of 2.2 mV/cm, followed by a secondary pulse (negative) with a pulse duration of 5.2 usec and an induced peak voltage of .3 mV/cm. The fields of both units were mapped with a search coil and were found to be homogeneous. Cells were cultured in flasks which were positioned either parallel to or transverse to the coils within the center of the field. Control flasks of aliquots of the same cells were cultured in the same incubator at least 3 m distance from the coils. Flasks were seeded with 4×10^4 cells. Mitotic activity was determined by counting tritium labeled thymidine incorpo-

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ration in cells 18 hr after thymidine introduction to flasks. Proliferation was determined after either 7 or 13 days of continuous exposure to the fields. After 7 days, Units 1 and 2 showed a positive response (31% and 47%, respectively). After 13 days, cells showed a lesser response to Unit 1 (-5.98%) and a slightly positive response to Unit 2 (10.04%). The differences in response indicate that signal configurations play a significant role in determining the responsiveness of fibrocytes.

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